

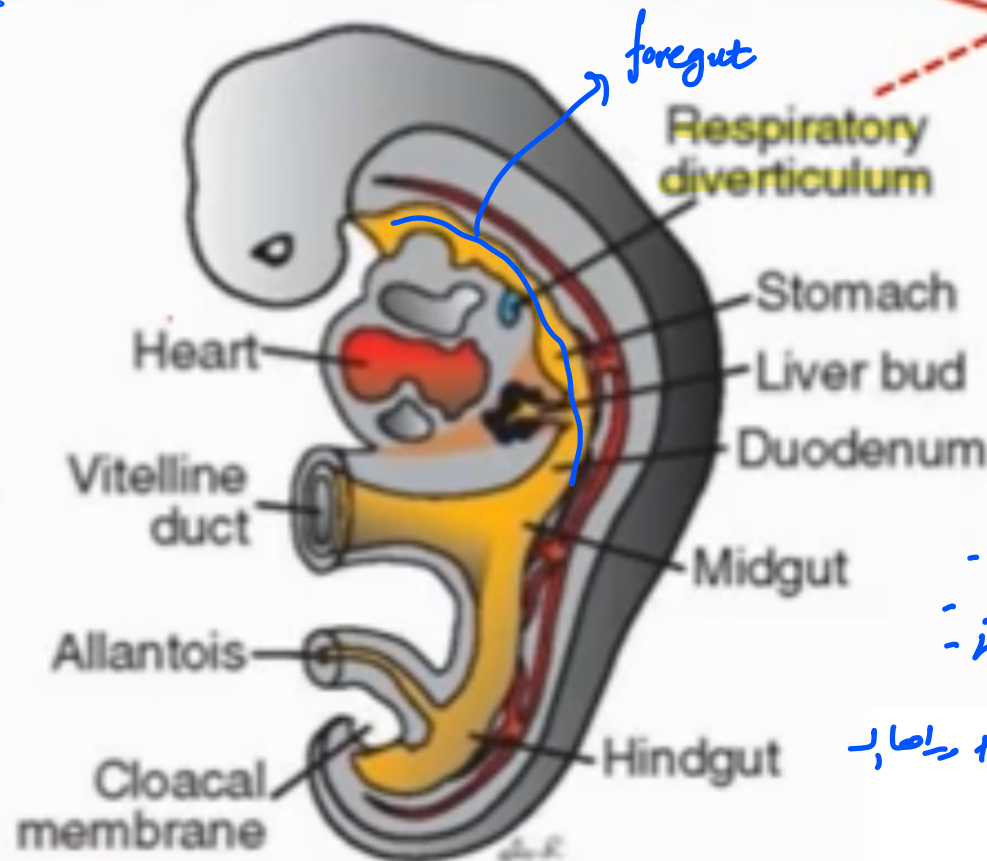
Respiratory Embryology

E J Arteen
FRCSI

The lung buds form during the 4th week

respiratory system

لے اہم مراقبہ ہے



foregut

Respiratory diverticulum

Heart

Stomach

Liver bud

Duodenum

Vitelline duct

Midgut

Allantois

Hindgut

Cloacal membrane

Langman's Medical Embryology, 10th ed

دستور ال
Lung buds
کے صیقل

Respiratory diverticulum *

تکبرہ سے جڑنے والا
(anterior)
ventral aspect of foregut.

- Foregut
- Midgut
- hindgut

* جڑنے والا GIT یہ ہوتا ہے

trachea، راسا،

* یعنی تکبرہ مقام، جڑنے
۔ esophagus

Lung buds

- Initially appear as the respiratory diverticulum, which is a ventral outgrowth of foregut endoderm

- MESODERM dependent process.**

* نتیجہ، foregut سے، middle of the 2nd part of duodenum
رہیگا، Midgut سے نتیجہ، junction سے،
Transverse colon، proximal 2/3، distal 1/3،
رہیگا، Hindgut۔

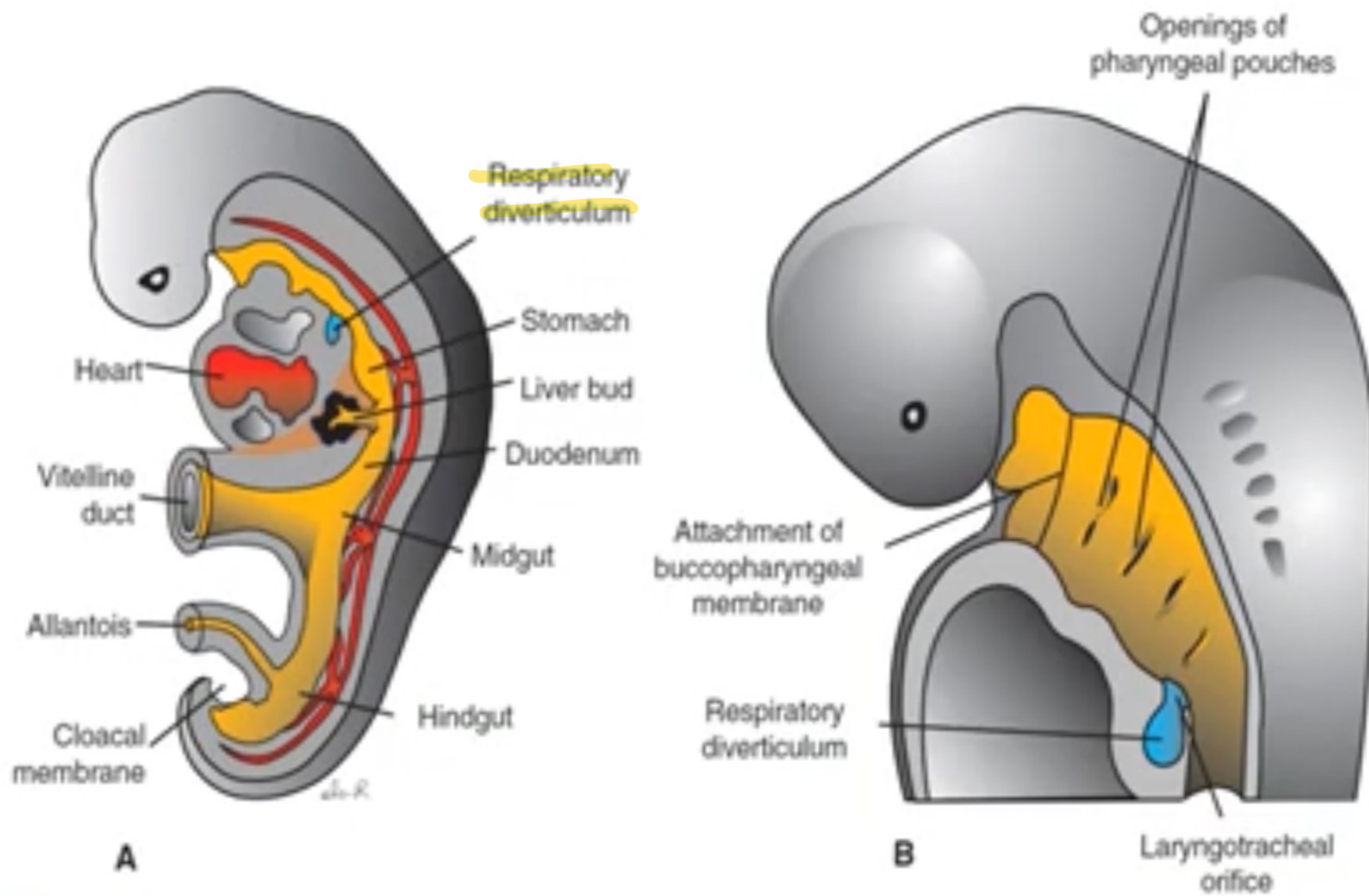


Figure 14.1 **A.** Embryo of approximately 25 days' gestation showing the relation of the respiratory diverticulum to the heart, stomach, and liver. **B.** Sagittal section through the cephalic end of a 5-week embryo showing the openings of the pharyngeal pouches and the laryngotracheal orifice.

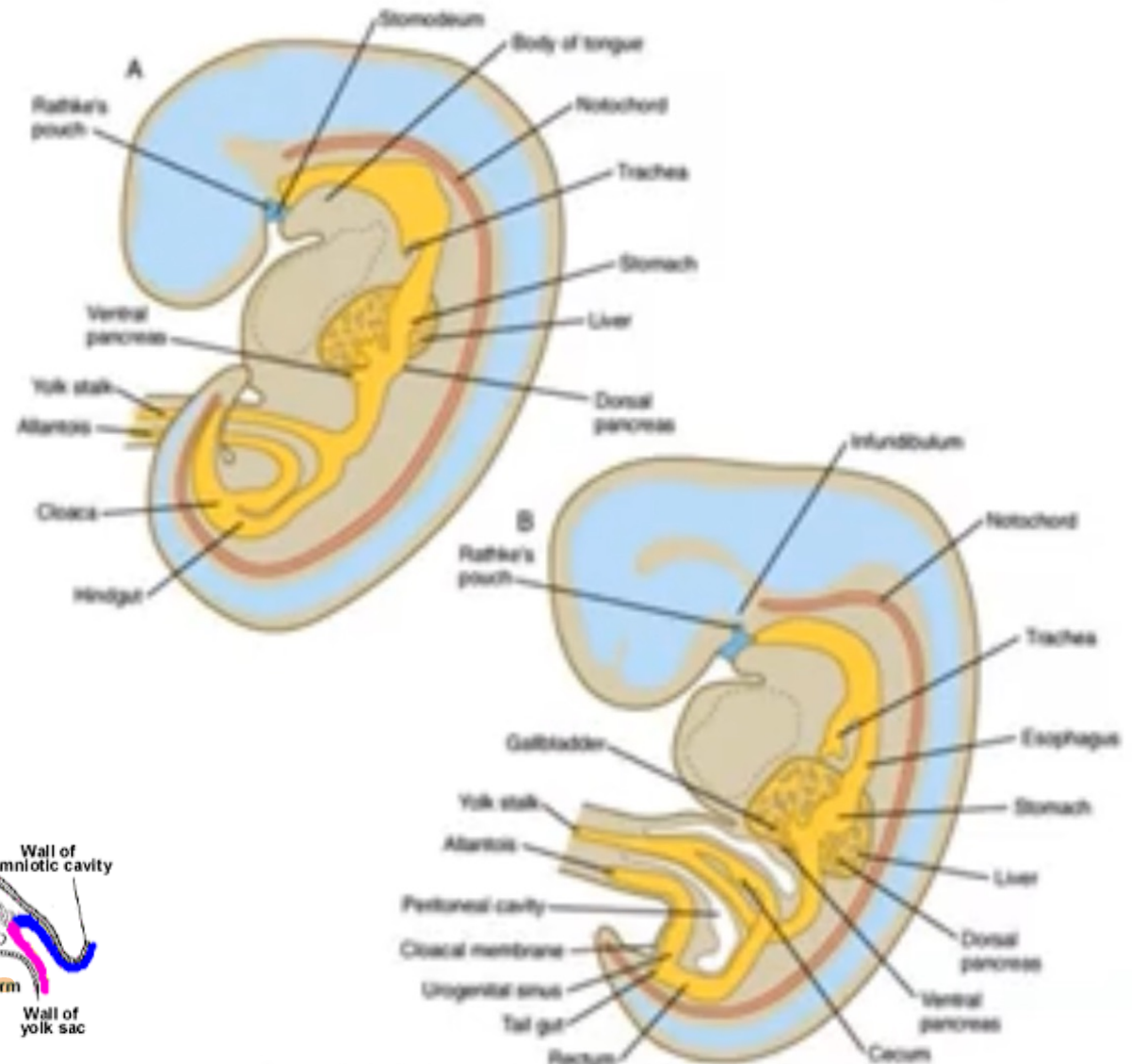
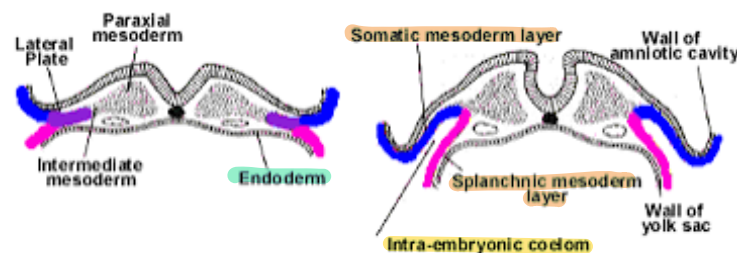
✕ The respiratory tract is derived from foregut endoderm and associated mesoderm

From endoderm:

epithelial lining of trachea, larynx, bronchi, alveoli

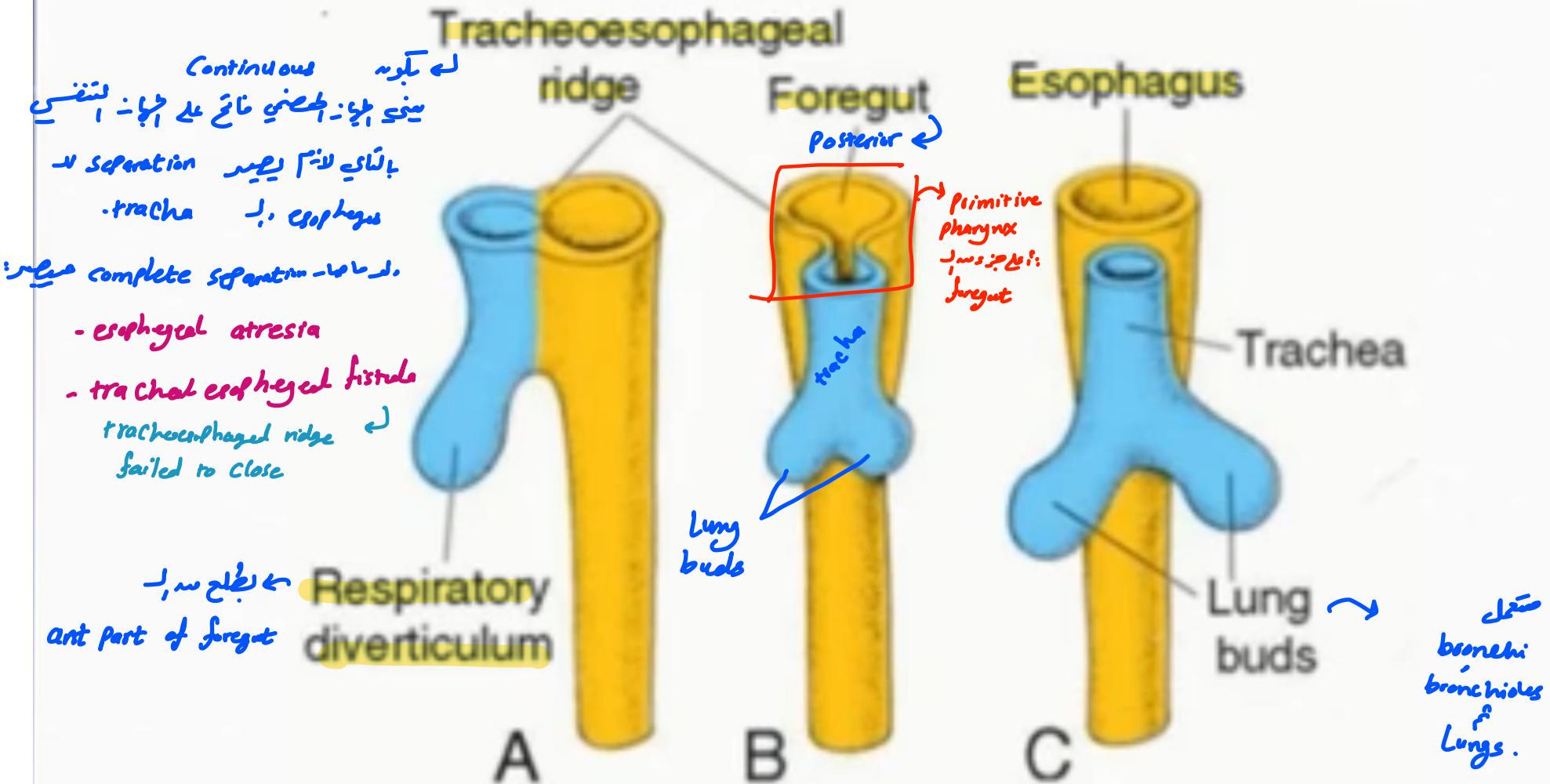
From splanchnic mesoderm:

cartilage, muscle, and connective tissue of tract and visceral pleura.



Carlson: Human Embryology and Developmental Biology, 4th Edition.
Copyright © 2009 by Mosby, an imprint of Elsevier Inc. All rights reserved.

Splitting of foregut into esophagus and trachea

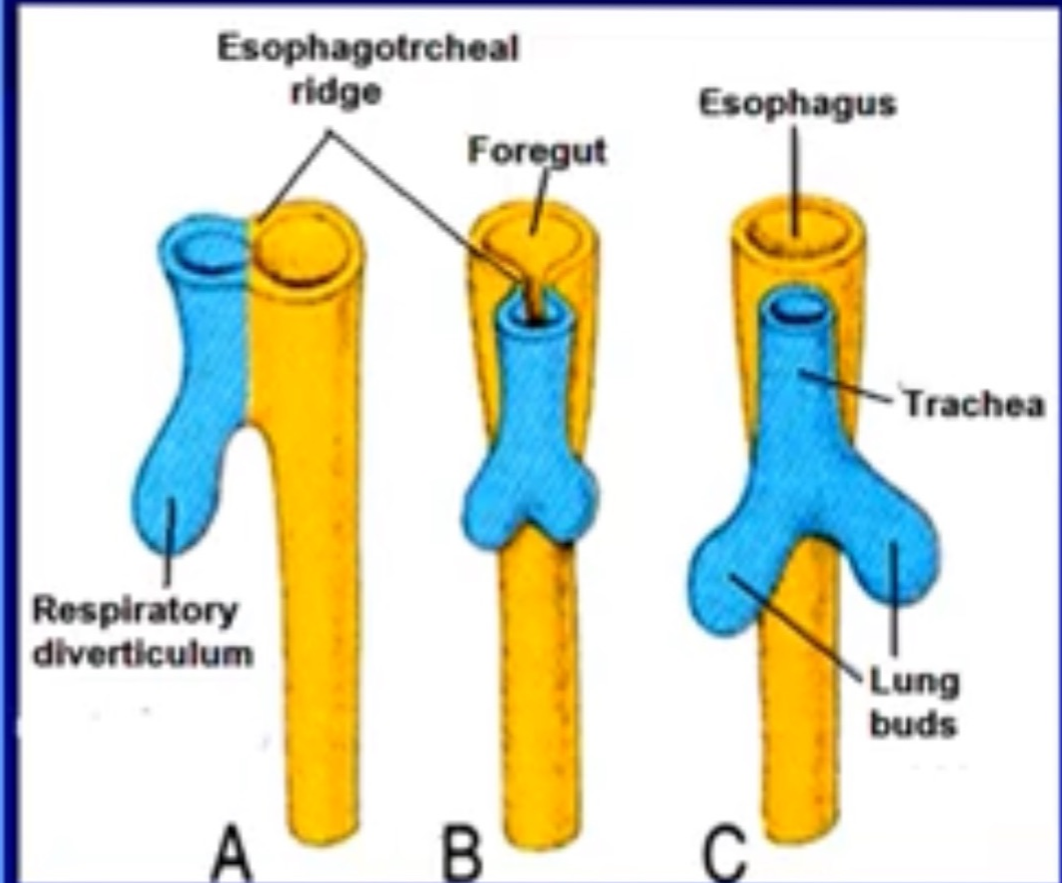


Tracheo-esophageal ridges: longitudinal ridges that eventually fuse to separate trachea from esophagus.

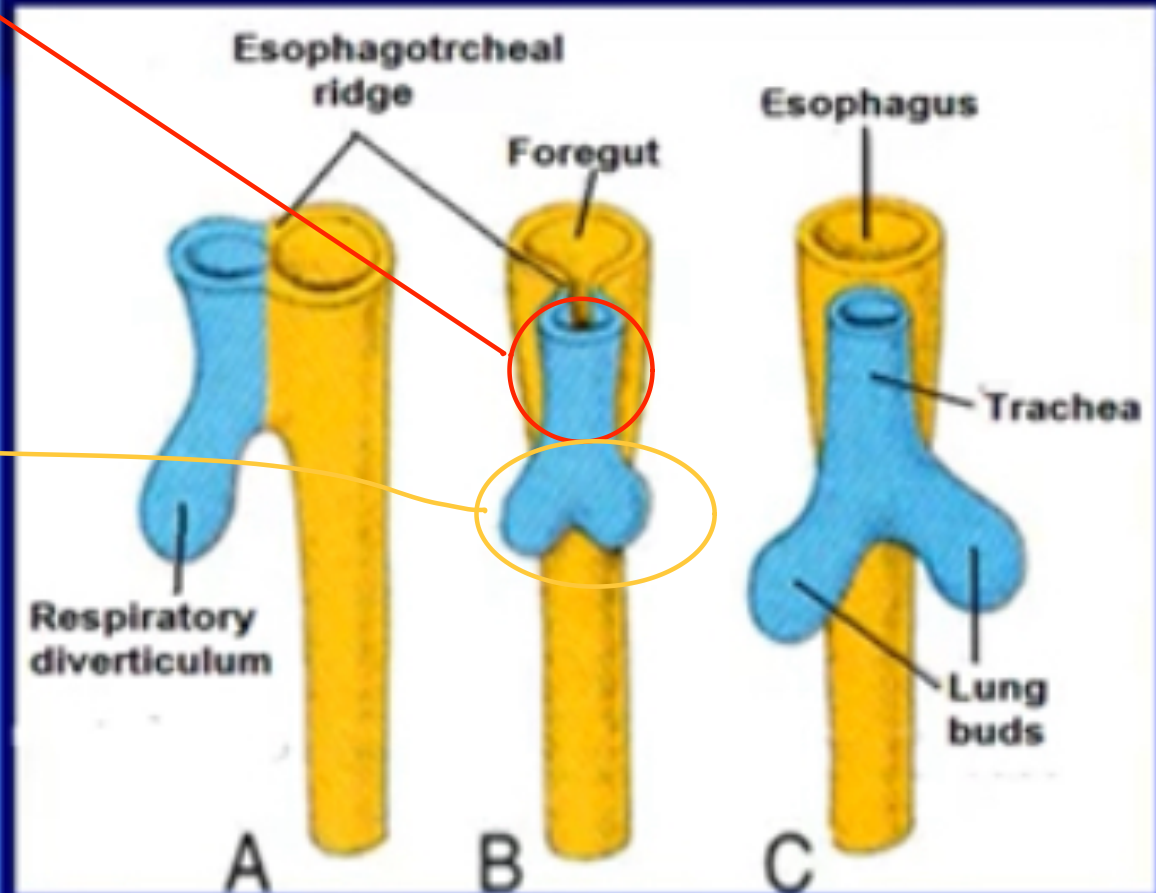
- A longitudinal **trachea - esophageal septum** develops and divides the diverticulum into a:

- **Dorsal portion:** ^{القناة الصفراء}
primordium of the oropharynx and ^(digestive system) esophagus

- **Ventral portion:** ^{الأنزعة}
primordium of larynx, trachea, bronchi and lungs ^(respiratory system)



- The proximal part of the **respiratory diverticulum** remains tubular and forms **larynx** & **trachea**.
- The **distal end** of the diverticulum dilates to form **lung bud**, which divides to give rise to **2 lung buds** (primary bronchial buds)
 - main bronchi



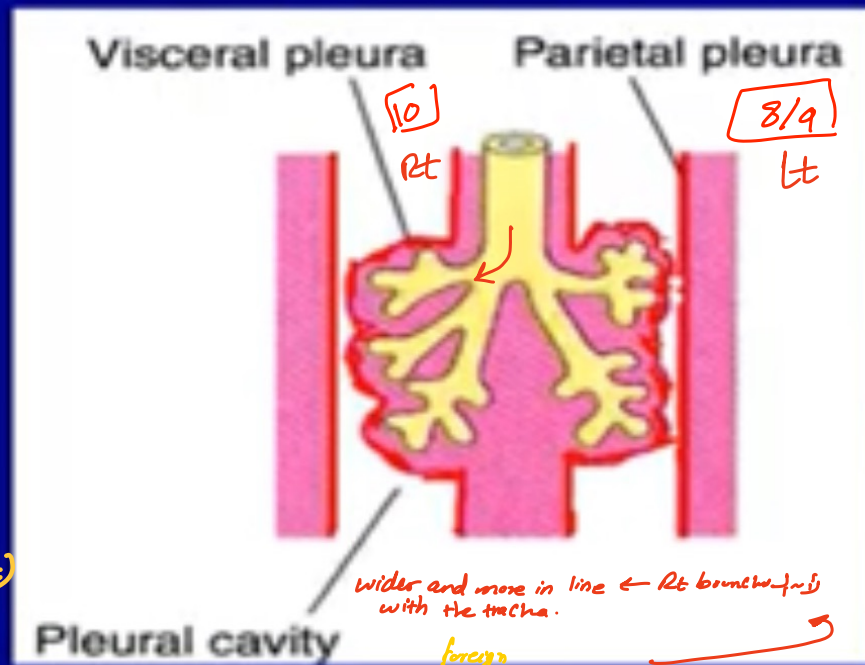
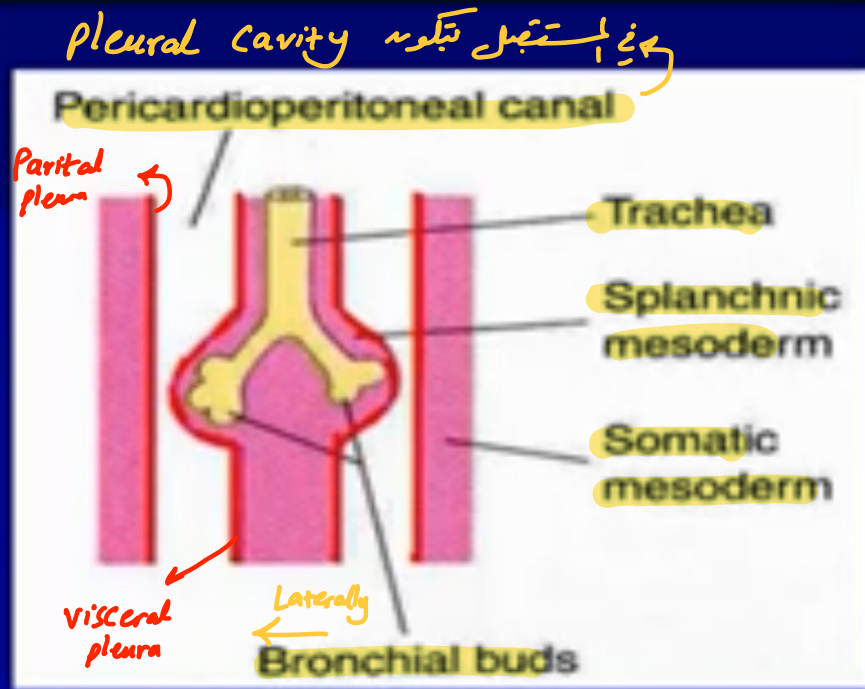
→ Rt / Lt →

2 bronchi
 ↓
 20 bronchi (Lobar bronchi)
 ↓
 3ry bronchi = bronchi Pulmonary segment

Development of the Bronchi & Lungs

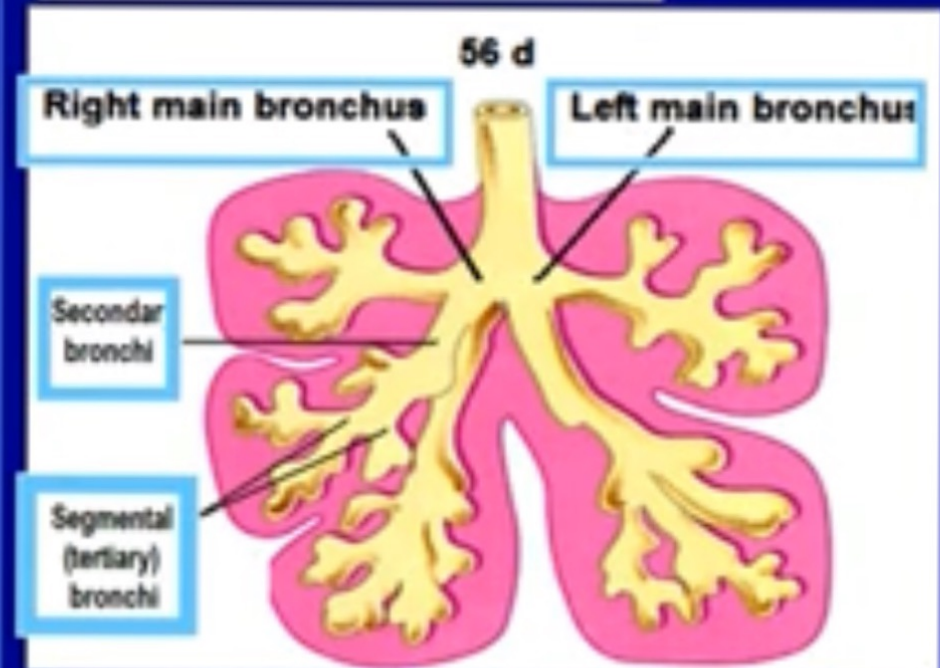
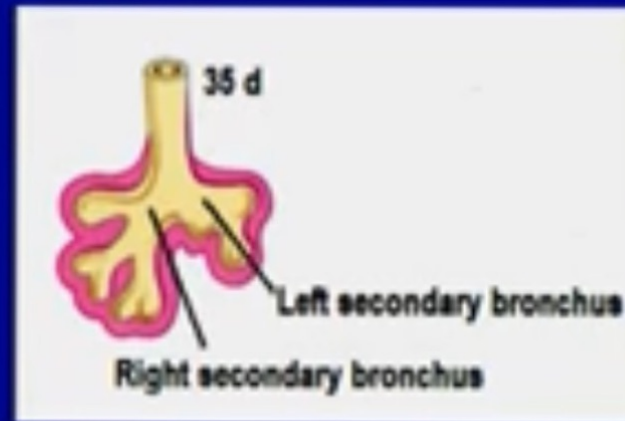
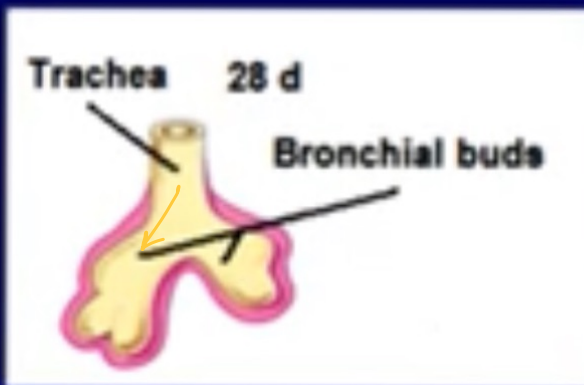
- The 2 primary bronchial buds grow laterally into the pericardio-peritoneal canals (part of the intraembryonic celome), the primordia of pleural cavities. *parietal and visceral pleura*
- Bronchial buds divide and redive to give the bronchial tree.

main bronchus → 2° bronchus → 3° bronchus
 Rt Lung [3] ← "lobar bronchus"
 Lt Lung [2] ← "branch. pulmonary segment"
 Rt → Lt
 upper lobe 3, middle lobe 2, lower lobe 3, upper lobe 4, lower lobe 4



صادق divison نفس الی ہے + اسکا وہاں ملتا ہے اندھا رج کے lung Rt →

- The right main bronchus is slightly larger than the left one and is oriented more vertically *عنا - صيد - foreign body*
- The embryonic relationship persists in the adult.
- The main bronchi subdivide into secondary and tertiary (segmental) bronchi which give rise to further branches. *لے کما - تقسم*

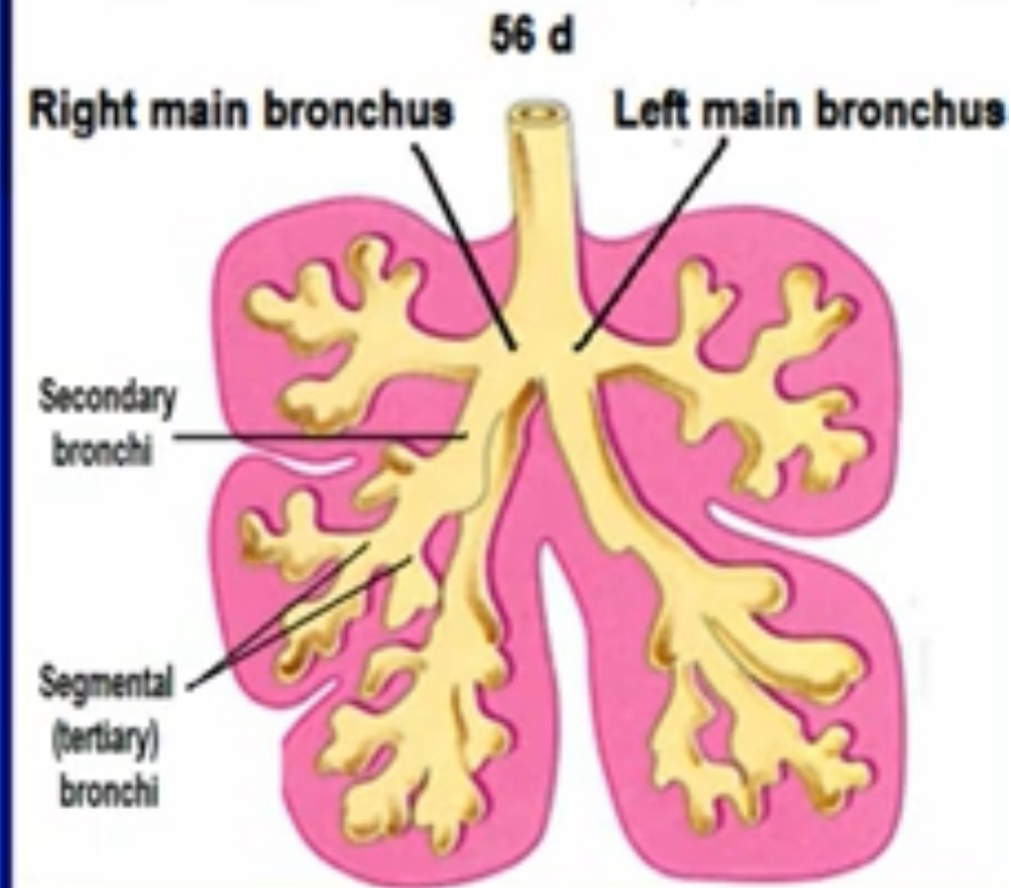


- **The segmental bronchi, 10 in right lung and 8 or 9 in the left lung begin to form by the 7th week**

- The surrounding mesenchyme also divides.

- **Each segmental bronchus with its surrounding mass of mesenchyme is the primordium of a broncho-pulmonary segment.**

lung fig → is the part of the lung tissue and per segmental which supply.



■ 2. Lobar bronchi (2°):

■ 2 Lt. & 3 Rt.

■ 3. Segmental bronchi (3°):

■ 10 Rt **3** upper lobe,
2 mid lobe **5** lower lobe

■ 8 Lt **4** upper lobe **4** lower lobe

Bronchopulmonary segments:

ہر حصہ شریانی ہے tumor سے لگتا ہے، مگر ماحول سے

■ Segmental bronchus and

pyramidal area of lung it

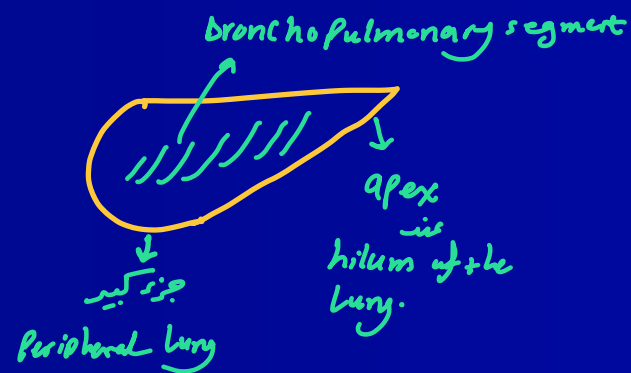
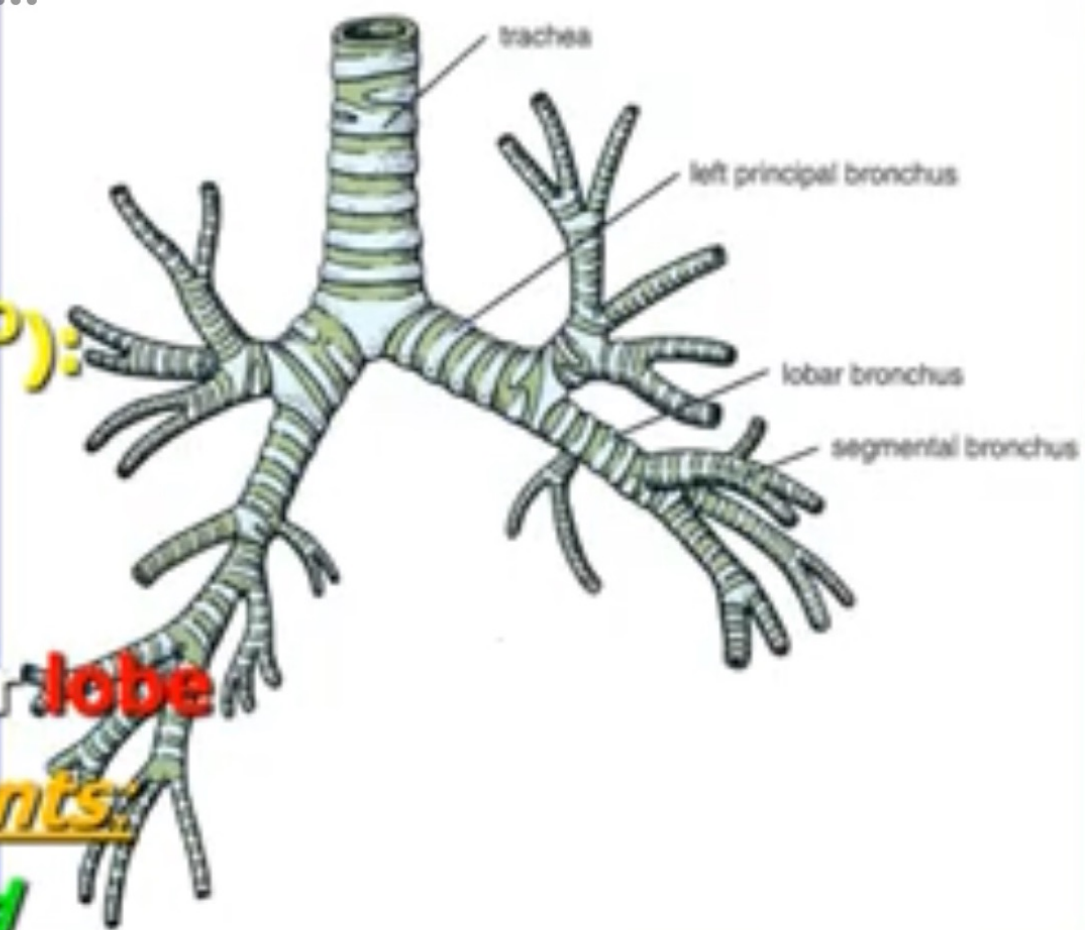
supply with apex at hilum,

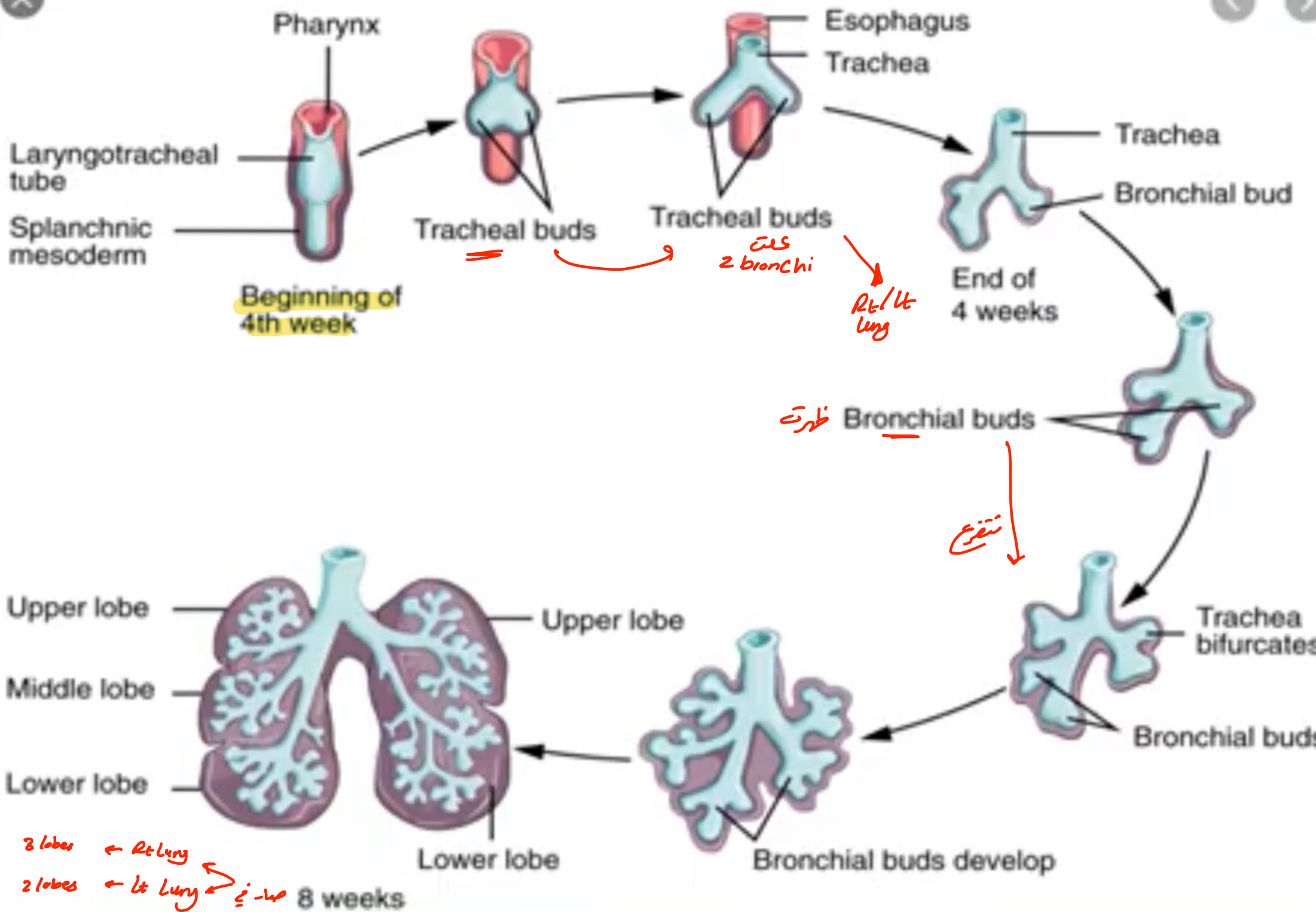
base at surface of lung, and

accompanying PA branch.

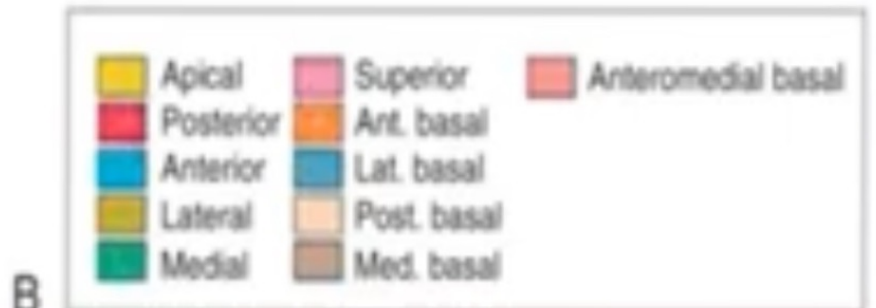
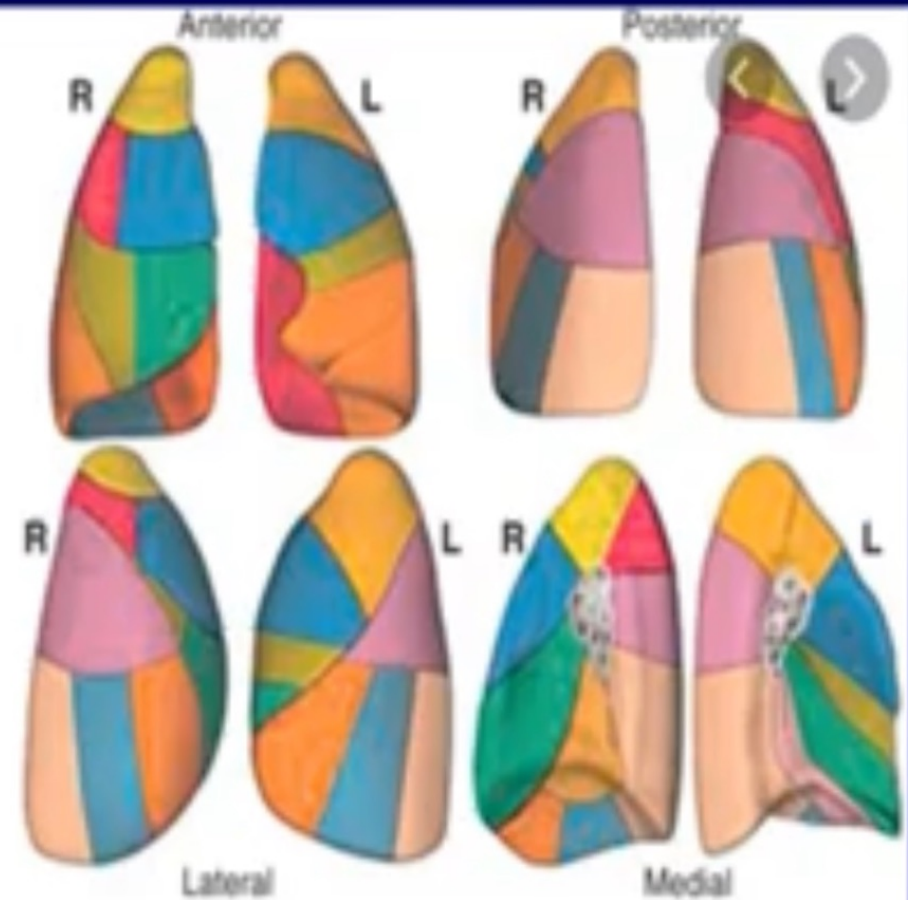
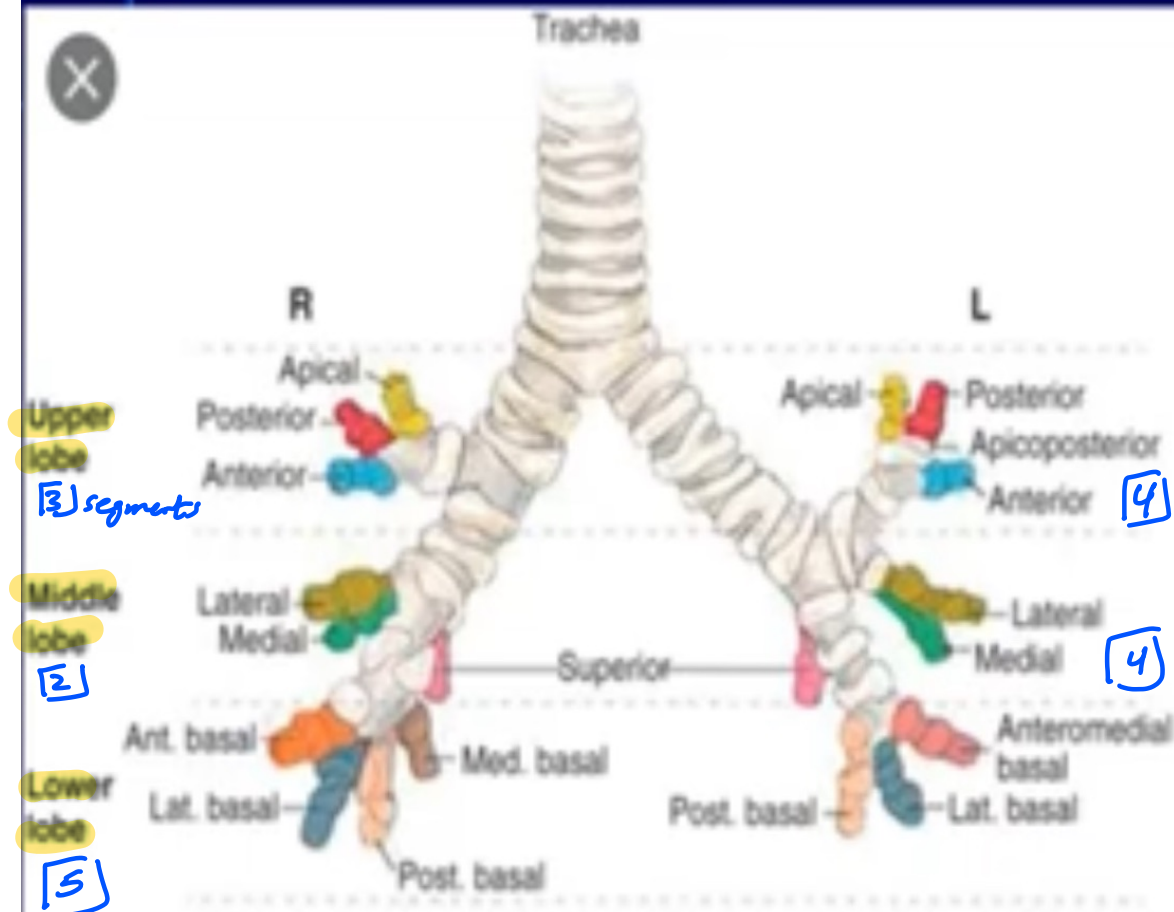
separate blood supply ہا *

↓
Pulmonary artery
+
Pulmonary vein





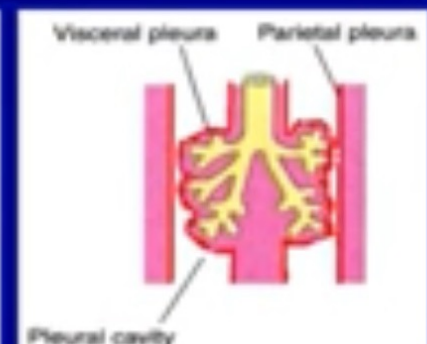
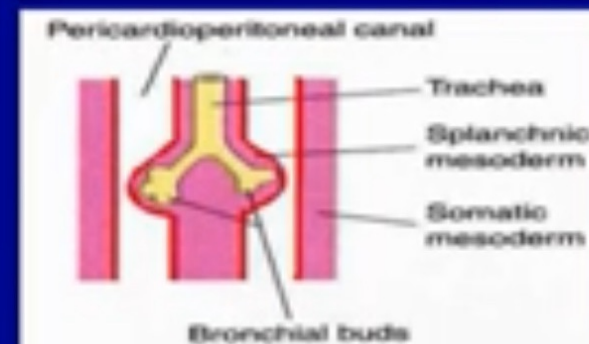
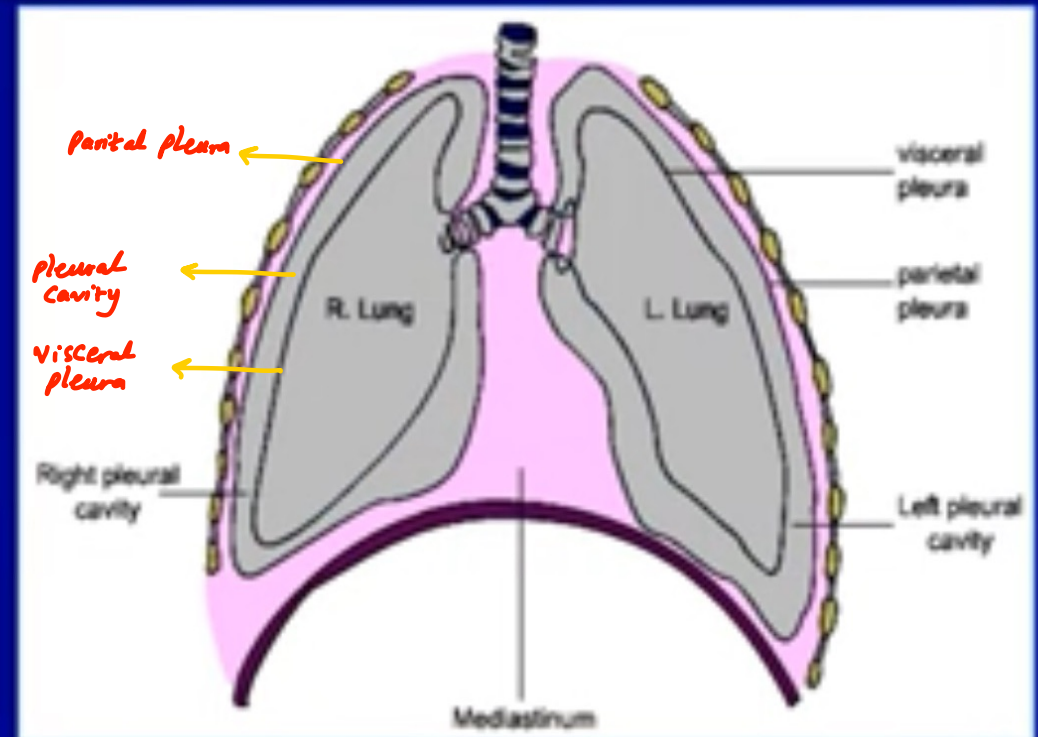
Bronchopulmonary segments:



- **By 24 weeks**, about **17** orders of branches have formed and **respiratory bronchioles** have developed.
- An additional **seven orders of airways** develop **after birth.** → = 24 orders

As the lungs develop they acquire a layer of **visceral pleura** from **splanchnic mesenchyme**.

The thoracic body wall becomes lined by a layer of **parietal pleura** derived from the **somatic mesoderm**.



Maturation of the Lungs

له مدة متداخلة

overlapped ← يعني ليست ترتيبية تبدأ الأولى وتخلص ويبدأ الثانية، ممتدة تتركب من آخر الأولى بأولى الثانية

■ Maturation of lung is divided into 4 periods:

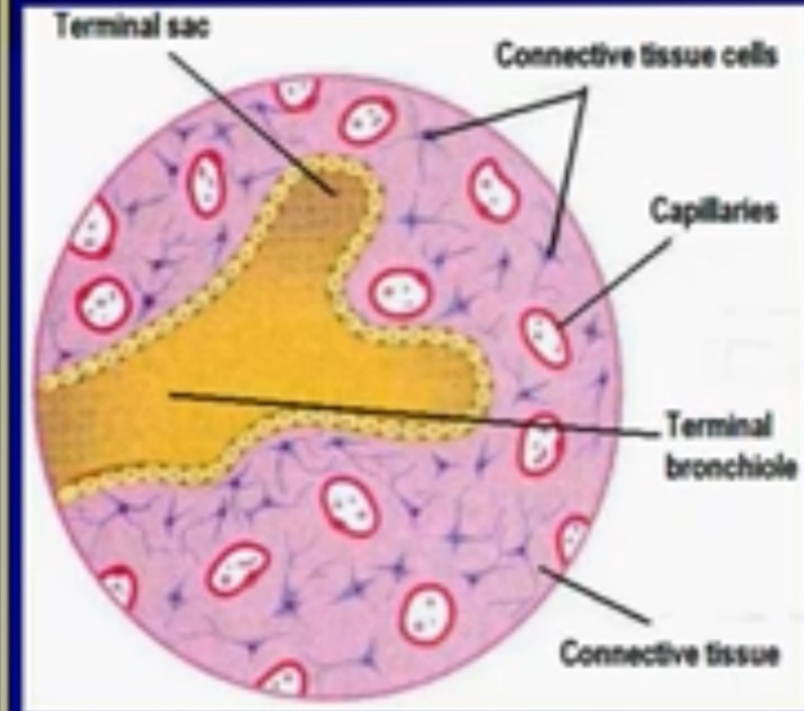
- Pseudoglandular (5 - 17 weeks) ≈ الشهر الرابع
 - Canalicular (16 - 25 weeks) → 4th - 6th
one week overlap
 - Terminal sac (24 weeks - birth) 6th - birth
32 weeks
 - Alveolar (late fetal period - childhood) 8th - 8 years
- These periods overlap each other because the cranial segments of the lungs mature faster than the caudal ones.

تقريباً عند الشهر الرابع

Pseudoglandular Period (5-17 weeks)

لے قبل 17 weeks ← Lung مشدنیڈ حایة تحمل سے gas exchange (Respiratory alveoli)
لے بالائی بعد 17 weeks ہے ای بیبی بنولہ جوتے۔

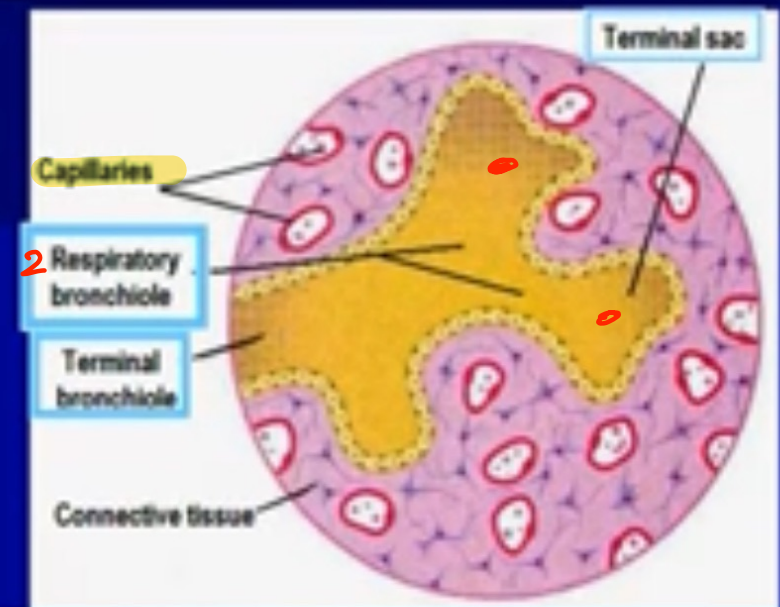
- Developing lungs somewhat resembles an exocrine gland during this period.
- By **17 weeks** all major elements of the lung have formed except **those involved with gas exchange (alveoli)**.
- Respiration is **NOT** possible.
- **Fetuses born during this period are unable to survive.**



→ They die

Canalicular Period (16-25 weeks)

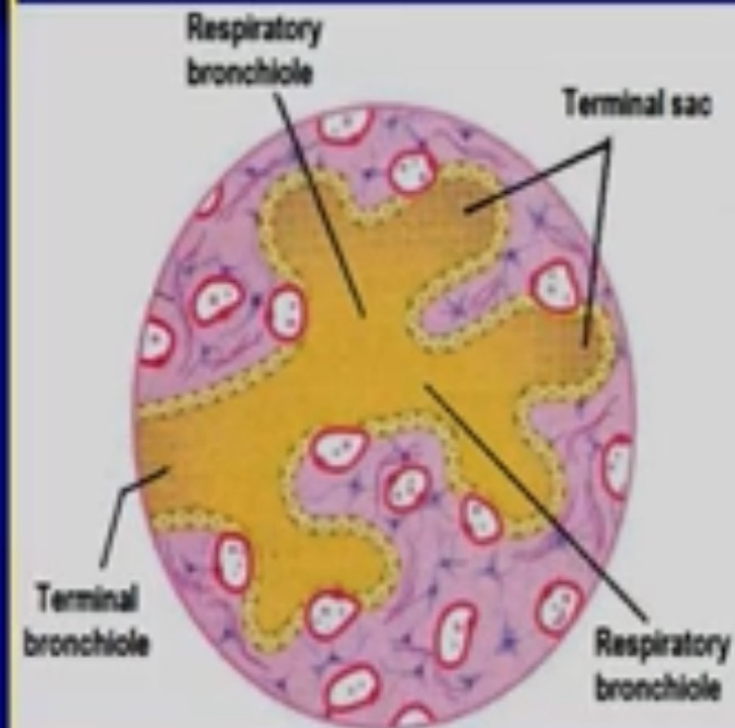
- Lung tissue becomes **highly vascular**. ^{gas exchange} ^{نزداد عشاء - لیبر} ^{capillaries}
- Lumina of **bronchi** and **terminal bronchioles** become larger.
- **By 24 weeks** each **terminal bronchiole** has given rise to two or more **respiratory bronchioles**.
- The **respiratory bronchioles** divide into 3 to 6 tubular passages called **alveolar ducts**.
- **Some** thin-walled **terminal sacs (primordial alveoli)** ^{تسلیس} ^{gas exchange} develop at the end of **respiratory bronchioles**.



- **Respiration is possible** at the end of **this period**.
- **Fetus** born at the end of this period may survive if given intensive care (but usually die because of the immaturity of respiratory as well as other systems)

Terminal Sac Period (24 weeks - birth)

- **Many more terminal sacs develop.**
- **Their epithelium becomes very thin.**
- **Capillaries begin to bulge into developing alveoli.**
- The epithelial cells of the **alveoli** and the endothelial cells of the **capillaries** come in intimate contact and establish the **Blood-Air barrier**. *"gas exchange between respiratory alveoli and capillary"*
- **Adequate gas exchange can occur which allows the prematurely born fetus to survive**



By ^{the end} **24 weeks**, the **terminal sacs** are lined by:

- Squamous **type I pneumocytes** and ^{were gas exchange occur}
- Rounded secretory, **type II pneumocytes**, that secrete a mixture of phospholipids called **surfactant**.

← نقيط Surface tension على ناميات عشاء زبيري ال Collapse
 ← نداشت surfactant ← يبق ناميات ← collapsed ← نداشت gas exchange ← ممتدة عذرة baby

- **Surfactant** production **begins** by 20 weeks and **increases** during the terminal stages of pregnancy.

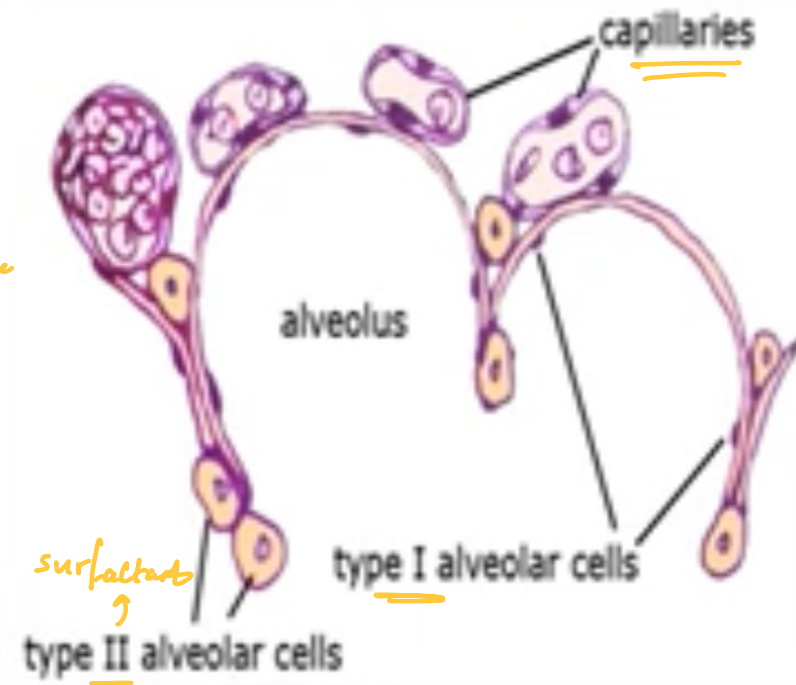
- **Sufficient terminal sacs, pulmonary vasculature & surfactant** are present to permit survival of a prematurely born infants ^{usually survive}

- Fetuses born prematurely at 24-26 weeks may ^{صعوبة التنفس} suffer from **respiratory distress** due to **surfactant deficiency** but **may survive** if ^{على حسب ICU و experience of the pediatrician} given **intensive care**.

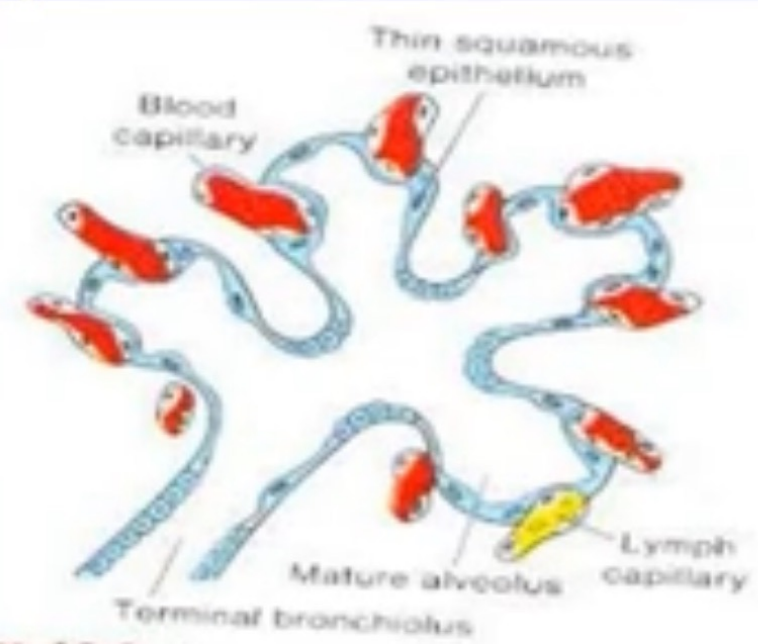
Alveolar Period (32 weeks – 8 years)

- At the beginning of the alveolar period, **each respiratory bronchiole terminates in a cluster of thin-walled terminal sacculles**, separated from one another by loose CT.

* بکریں موجود
blood capillaries
+
alveoli
+
proper gas exchange



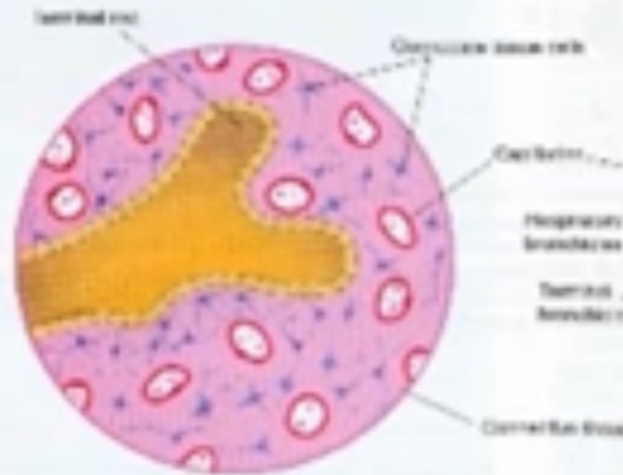
- These terminal sacculles represent future alveolar sacs.
- The epithelial lining of the terminal sacs attenuates to an extremely **thin squamous epithelial layer**.



Stages of Maturation of the Lungs

① Pseudoglandular Period (5-17 weeks):

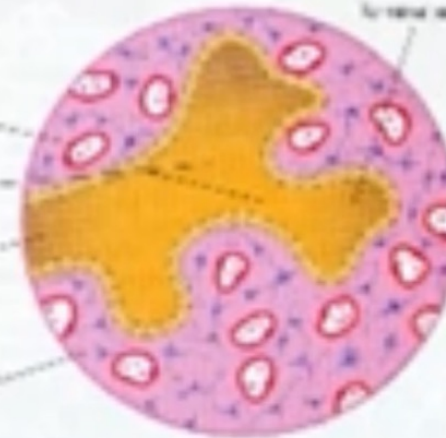
By 17 weeks, all major elements have formed, except those involved with gas exchange (fetuses unable to survive if born at this stage).



A Pseudoglandular period (5-17 weeks)

② Canalicular Period (16-25 weeks):

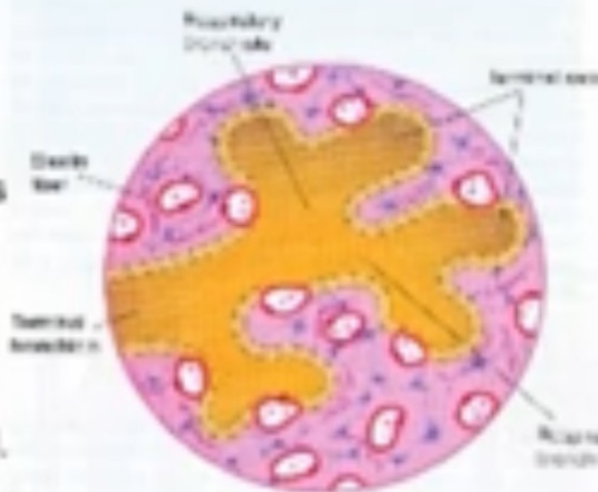
Bronchi, terminal bronchioles become larger, lung tissue becomes highly vascular. Alveolar ducts form by week 24. By end, some terminal sacs have formed so respiration is possible (small chance of survival at this stage).



B Canalicular period (16-25 weeks)

③ Terminal Sac Period (24 weeks to birth):

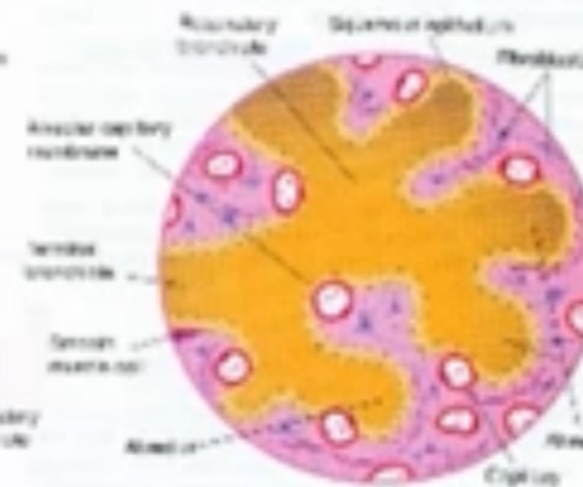
Many more terminal sacs develop, their epithelium becomes very thin and capillaries bulge into the developing alveoli. Blood-air barrier becomes well-developed. (By 26-28 wks, 1000 gr fetus has a sufficient # of sacs and surfactant to survive.)



C Terminal sac period (24 weeks to birth)

④ Alveolar Period (late fetal period to age 8):

Alveoli-like structures are present by 32 weeks. Epithelial lining of sacs attenuate to extremely thin squamous epithelia, capable of gas exchange. 95% of characteristic, mature alveoli develop after birth.



D Alveolar period (birth to 8 years)

- Characteristic mature alveoli do not form until after birth. 95% of alveoli develop postnatally. بعد الولادة

← عند الولادة

- About 50 million alveoli, one sixth of the adult number are present in the lungs of a full-term newborn infant.

- Most increase in the size of the lungs results from an increase in the number of respiratory bronchioles and primordial alveoli. rather than from an increase in the size of the alveoli.

- From 3-8 year or so, the number of immature alveoli continues to increase. Unlike mature alveoli, immature alveoli have the potential for forming additional primordial alveoli.

- By about the eighth year, the adult complement of 300 million alveoli is present.

← 8 سنوات عند الولادة

occur in fetus
 Lung
 placenta
 umbilical cord

۱. Lung تپکوه
۲. میانہ جاں
aminio
fluid
۳. رقی و بخل
Lung

■ Occur before birth, are not continuous and increase as the time of delivery approaches.

- Help in conditioning the respiratory muscles. *تنسيق عمل العضلات التنفسية*

- Stimulate lung development and are essential for normal lung development.

← الفصل الولد سیت
سأفقد نفسی
فما بال صبا

amniotic

2

This fluid in the lungs is cleared at birth: by: لَمَّا يَمُوتُ الْفَلَسُفُ وَتَنفَسُ عِنْدَ الْمِيلَادِ

- ◆ Pressure on the fetal thorax during delivery.
- ◆ Absorption into the pulmonary capillaries and lymphatics. *of the lung*

← للصب السري. Lungs of a Newborn

■ Fresh healthy lung always contains some air (lungs float in water).

Diseased lung may contain some fluid and may not float (may sink).

← Lungs of a stillborn infant are firm, contain fluid and may sink in water.

Gamnetic

ثقلية

Factors important for normal lung development

- Adequate thoracic space for lung growth.
- Fetal breathing movements. يتم عمل conditioning يتأثر به Lung تشكيل
- Adequate amniotic fluid volume. لأنه إذا قل يمتلئ بطغى Lung . يسهل على maturation

Developmental anomalies

Laryngeal atresia. obstruction of esophagus

Tracheoesophageal fistula. trachea فتحة على esophagus - فتحة مصدرة (fistula)

Tracheal stenosis & atresia.

Congenital lung cysts. Lung عيبات خلقية

Ageneis of lungs. = absent Lung or Lobe of Lung.

Lung hypoplasia. = small lung

Accessory lungs. ل. إضافية

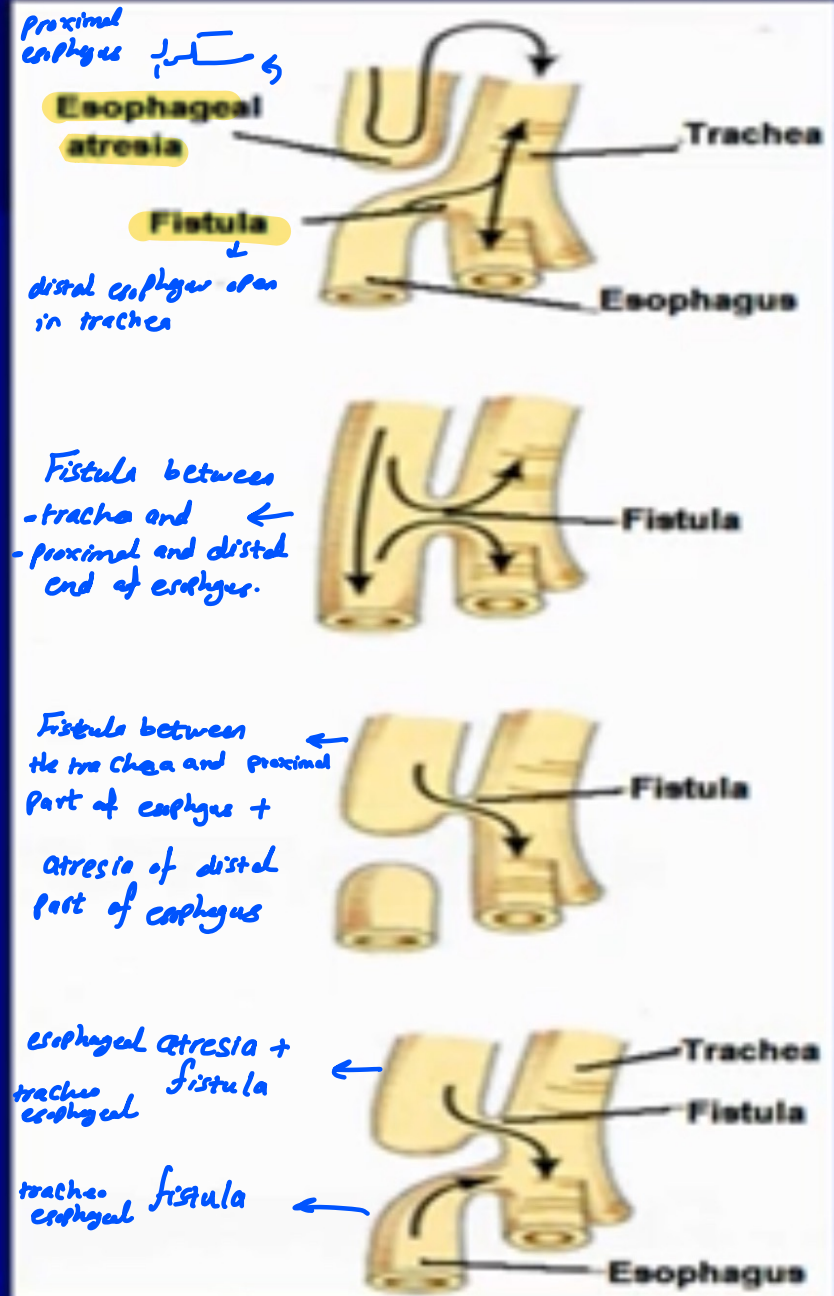
Tracheoesophageal Fistula

لأنه أنواع

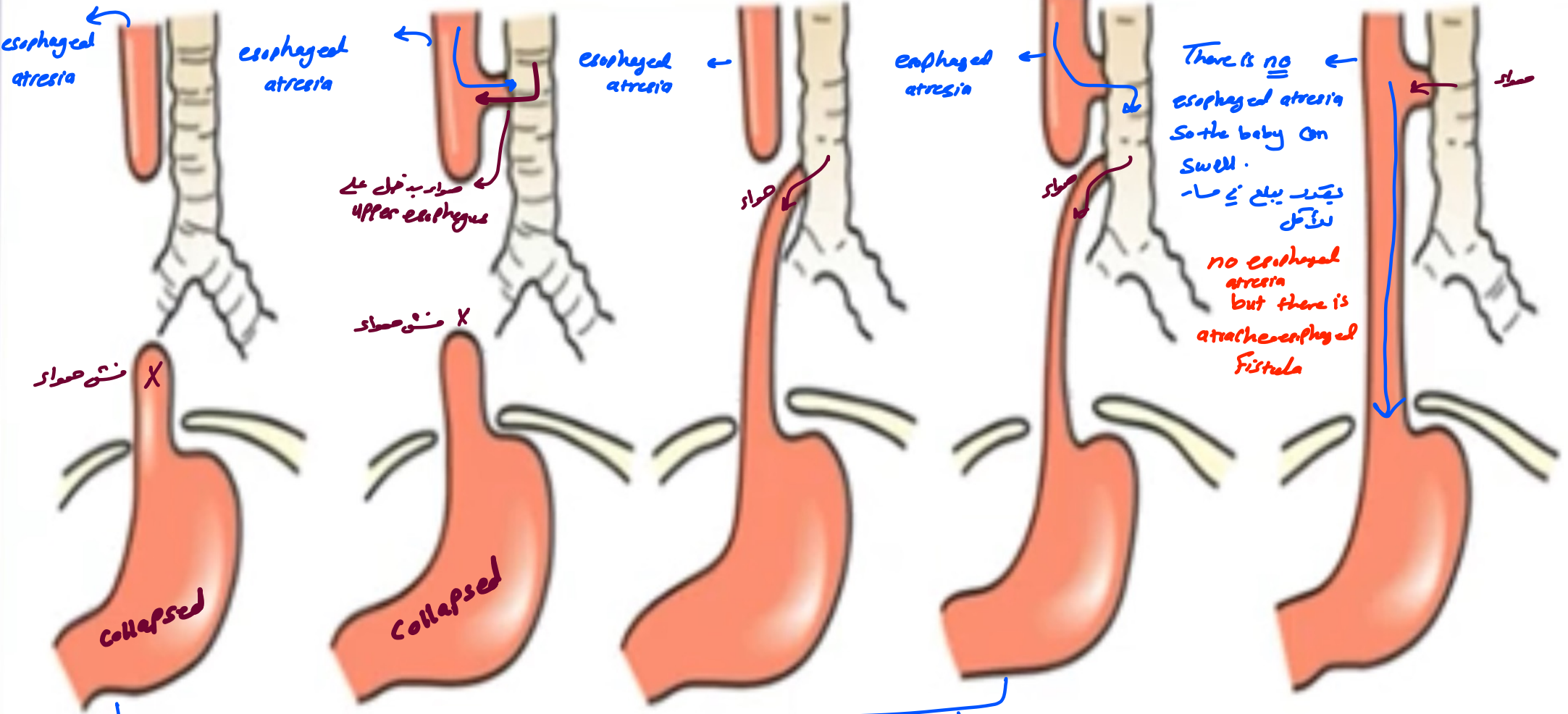
- An **abnormal passage** between the trachea and esophagus.
- Results from **incomplete division** of the cranial part of the foregut into respiratory and esophageal parts.
- Occurs once in 3000 to 4500 live births.
- Most affected infants are **males**.
- In more than **95% of cases**, the fistula is associated with **esophageal atresia**.

فistula بين trachea و esophagus

esophageal obstruction



+ atresia in the proximal part of esophagus
+ distal part of esophagus open in trachea



A 7%

isolated esophageal atresia

no fistula

B 2%

- proximal fistula
- distal atresia

FIGURE 66-6 Anatomical variants and incidence of esophageal atresia with tracheoesop...

C 86%

proximal → atresia
distal → fistula

aspiration
immediately
and 2-3 days of age, lung, trachea, and esophagus

D 1%

proximal part → atresia + fistula
distal part → fistula

عادةً عنفاً، الغلغلة، الموت
immediately

E 4%

* Fistula + atresia in proximal
→ die immediately
* lucky they are 3%

* سؤال

* ال Baby كجوه رطنه متنفخ ني آي انواع سنم ؟! "للتفريده بينهم :

متنفخ ← يعني gas يدخل على Stomach يعني لانم في طريقه للمواد على Stomach
↓
Sever abdominal distension.
مصني حالات C, D, E

متكجوه ال Stomach ← collapsed ← في حالات A, B نسبة ١٥٪ "gasless abdomen"

* حل ال esophageal atresia , tracheoesophageal fistula جصل طاله ؟

مرات جصل طاله كنه مرات كجوه مع other anomalies ، كتر اختصرواني

- Vater anomalies : [5]

- VACTERL anomalies : [7]

Tracheo-esophageal fistulas



- Incomplete separation and/or atresia of trachea and esophagus (*B on right shows esophageal atresia*)
- Defect likely in mesoderm and usually associated with other defects involving mesoderm (cardiovascular malformations, VATER / VACTERL, etc.)

Sanomiles

VATER = **V**ertebral anomalies, **A**nal atresia, **T**racheoesophageal fistula, **E**sophageal atresia, **R**enal atresia

VACTERL = VATER + **C**ardiac defects & **L**imb defects

↳

VACTERL Syndrome

5

Vertebral anomalies. *→ not well developed*

Anorectal malformation. *→ imperforate anus*

Cardiac anomalies.

→ *قائمة ما جمة تبقوه في +*
VACTERL anomalies + VSD + ASD + tetralogy of Fallot
متبقوه معها *ASD صداد انت تبقوه ASD*
"ventricular septal defect" *atrial septal defect*

Tracheo-esophageal fistula.

→ isolated

Esophageal atresia.

→ fistula يوصل

Renal anomalies.

→ kidney agenesis
= one kidney absent

Limb anomalies.

→ no radius bone
→ poly ductly / syndactyly اصبع ثنائي

* أي طفل عنده one anomaly

↓
بنه على other anomalies

له شدة عنده مشاغل في أصابع - جليه
نبتوله مع الحصى في heart عنده

Cardiac pediatric cardiology
عنده سائده فيه cardiac anomalies

وينجل ultrasound للقلب عنده
نشوفه في kidney موجوده

* So, if baby has one anomaly
he might has other.

Tracheo-esophageal fistulas

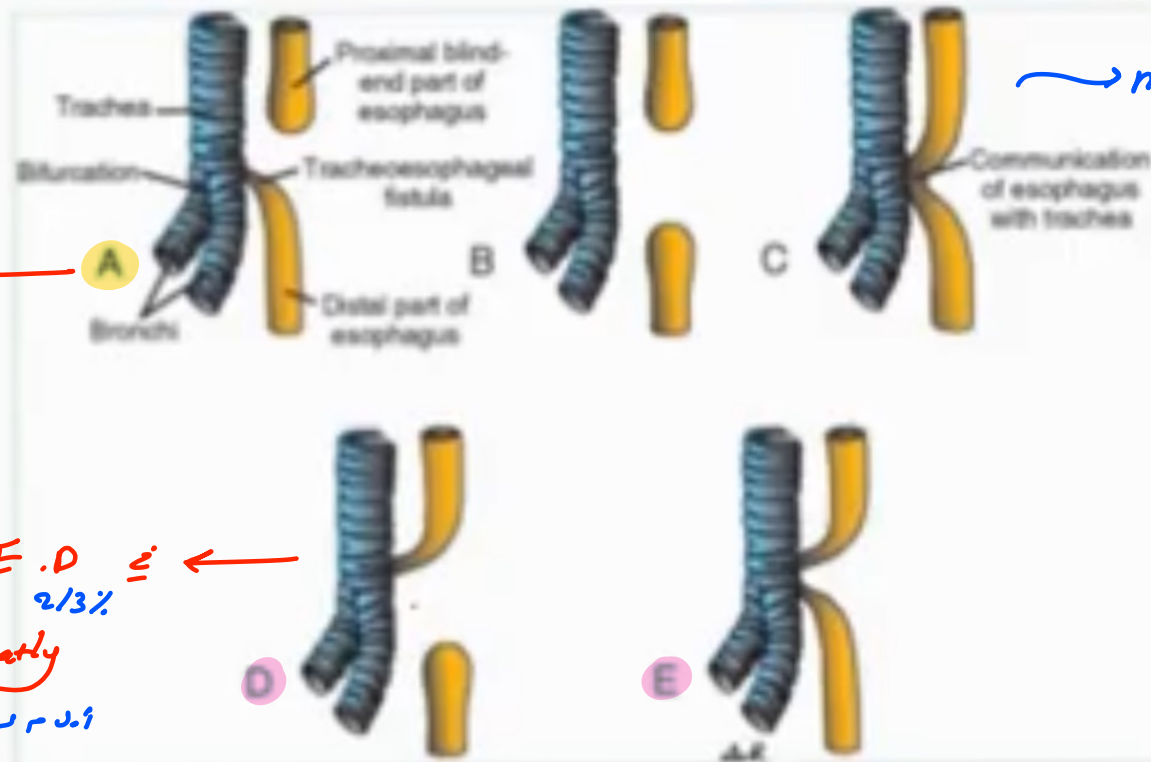


- Incomplete separation and/or atresia of trachea and esophagus (*B on right shows esophageal atresia*)
- Defect likely in mesoderm and usually associated with other defects involving mesoderm (cardiovascular malformations, VATER / VACTERL, etc.)

VATER = Vertebral anomalies, Anal atresia, Tracheoesophageal fistula, Esophageal atresia, Renal atresia

VACTERL = VATER + Cardiac defects & Limb defects

Tracheoesophageal Fistulas / Esophageal Atresia



no atresia but there is fistula.

The commonest
: proximal atresia
+
distal fistula

Proximal fistula : E.D 2/3%
↓
∴ Baby die immediately
عدم شرب صيد على lungs

- Occur in approx 1/3000 births, most (90%) are that shown in (A) above.

● Complications:

- PRENATAL: Polyhydramnios (due to inability to swallow amniotic fluid in utero)
- POSTNATAL

Gastrointestinal: Infants cough and choke when swallowing because of accumulation of excessive saliva in mouth and upper respiratory tract. Milk is regurgitated immediately after feeding.

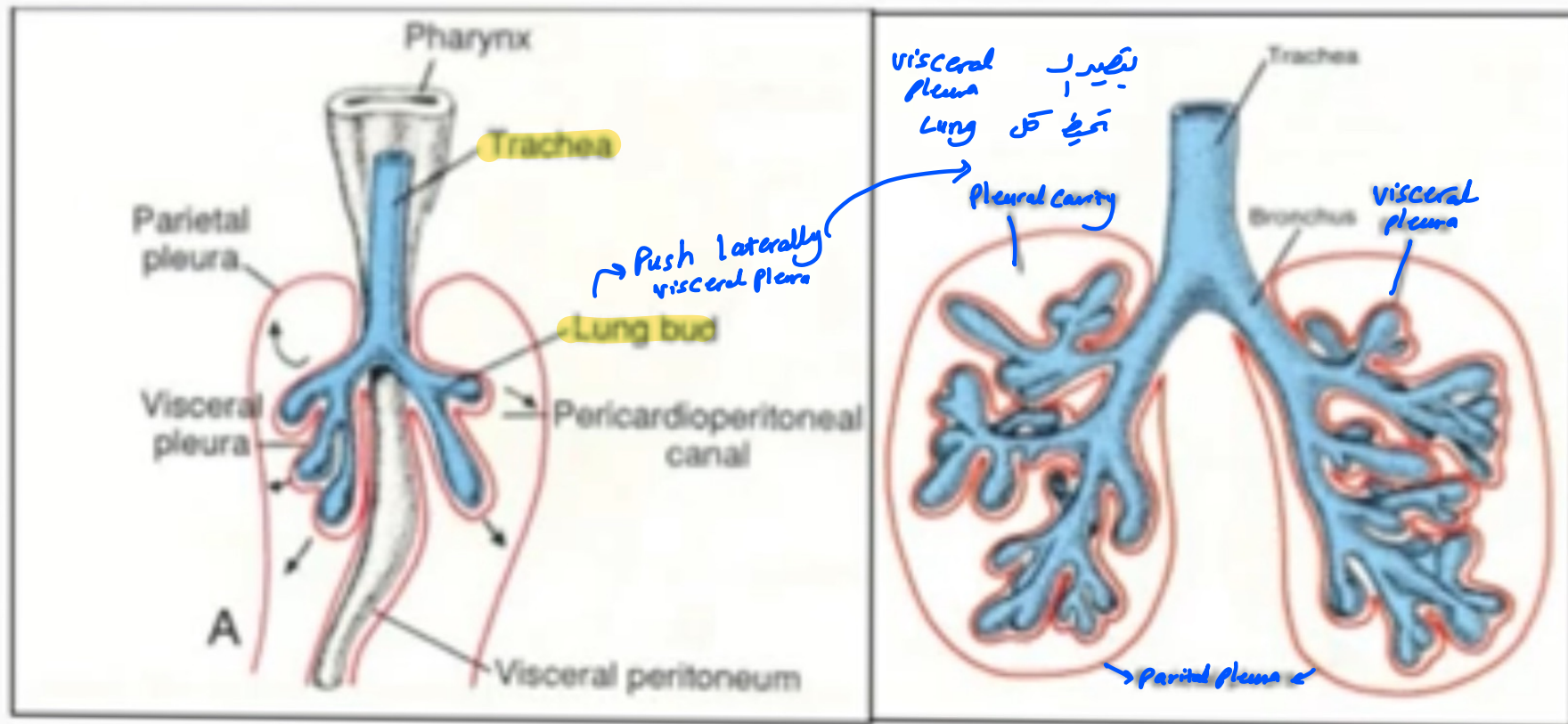
Respiratory: Gastric contents may also reflux into the trachea and lungs, causing choking and often leading to pneumonitis.

Differentiation of pleural membranes

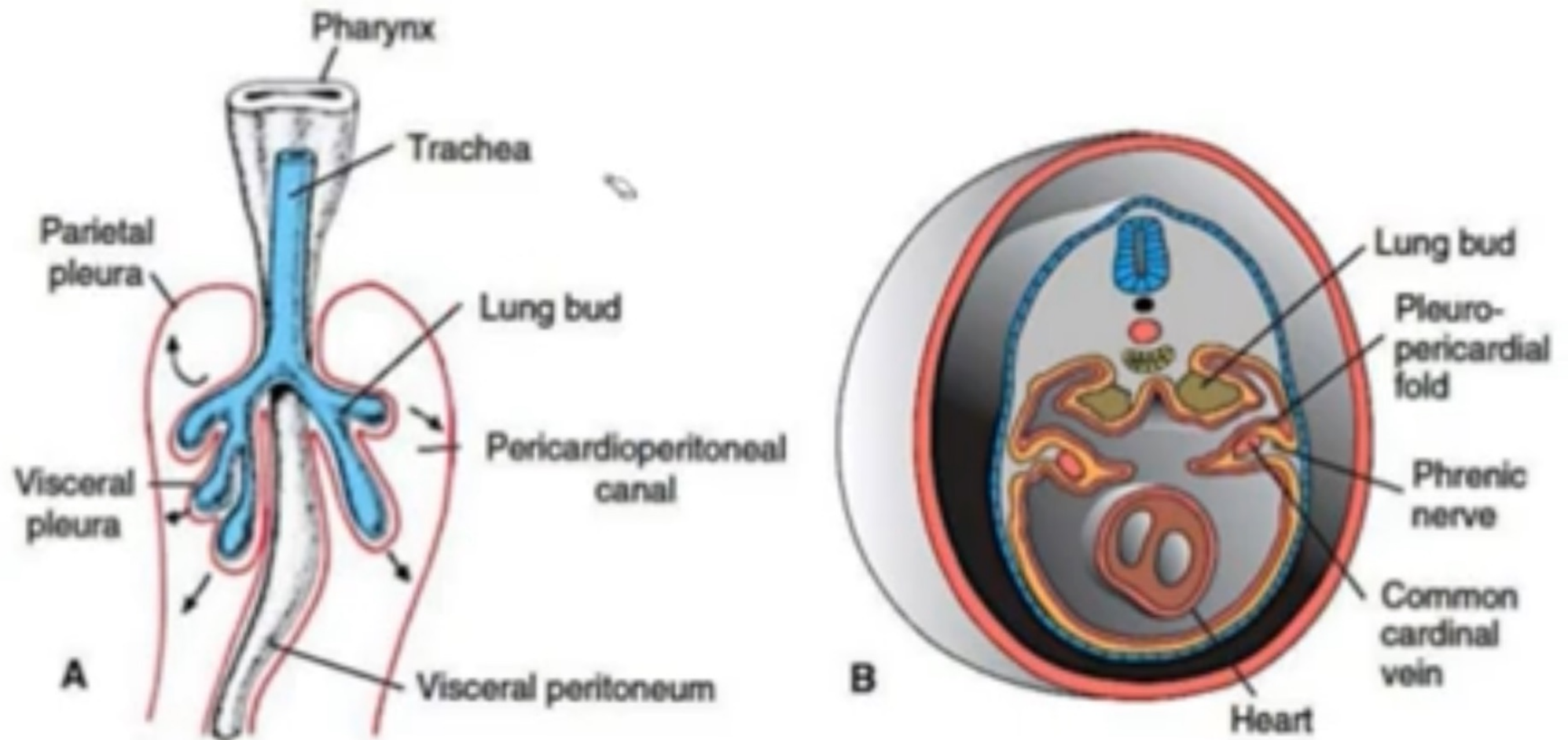
Laterally

لے نکال دے، organs بتدخول علیٰ Peritonium سے خلف

The lung buds "punch" into the visceral mesoderm. The mesoderm, which covers the outside of the lung, develops into the visceral pleura. The somatic mesoderm, covering the body wall from the inside, becomes the parietal pleura. The space between is the pleural cavity.



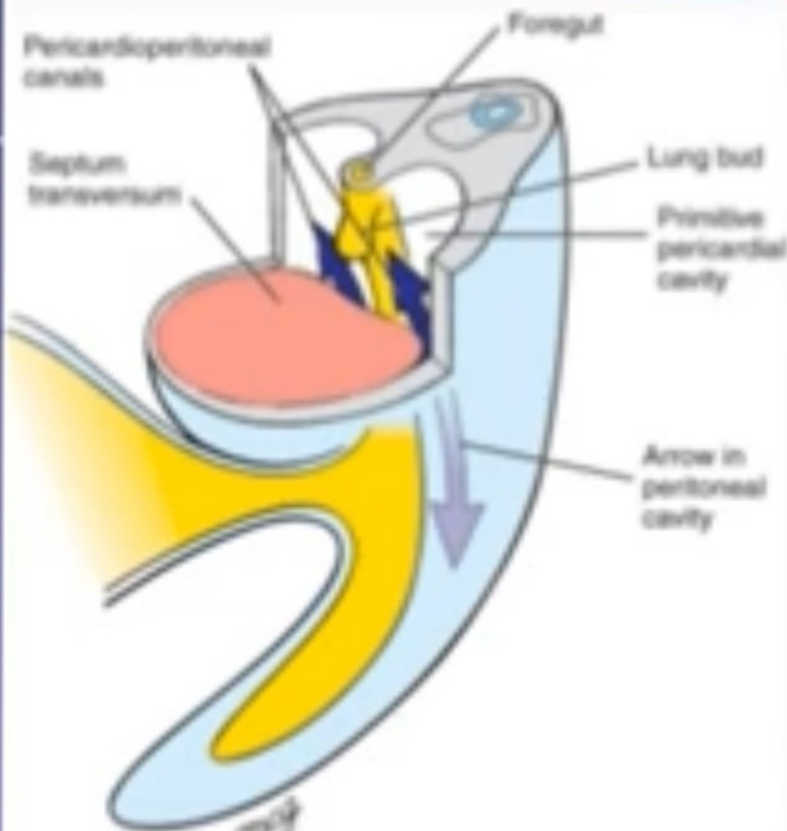
Pleural cavity



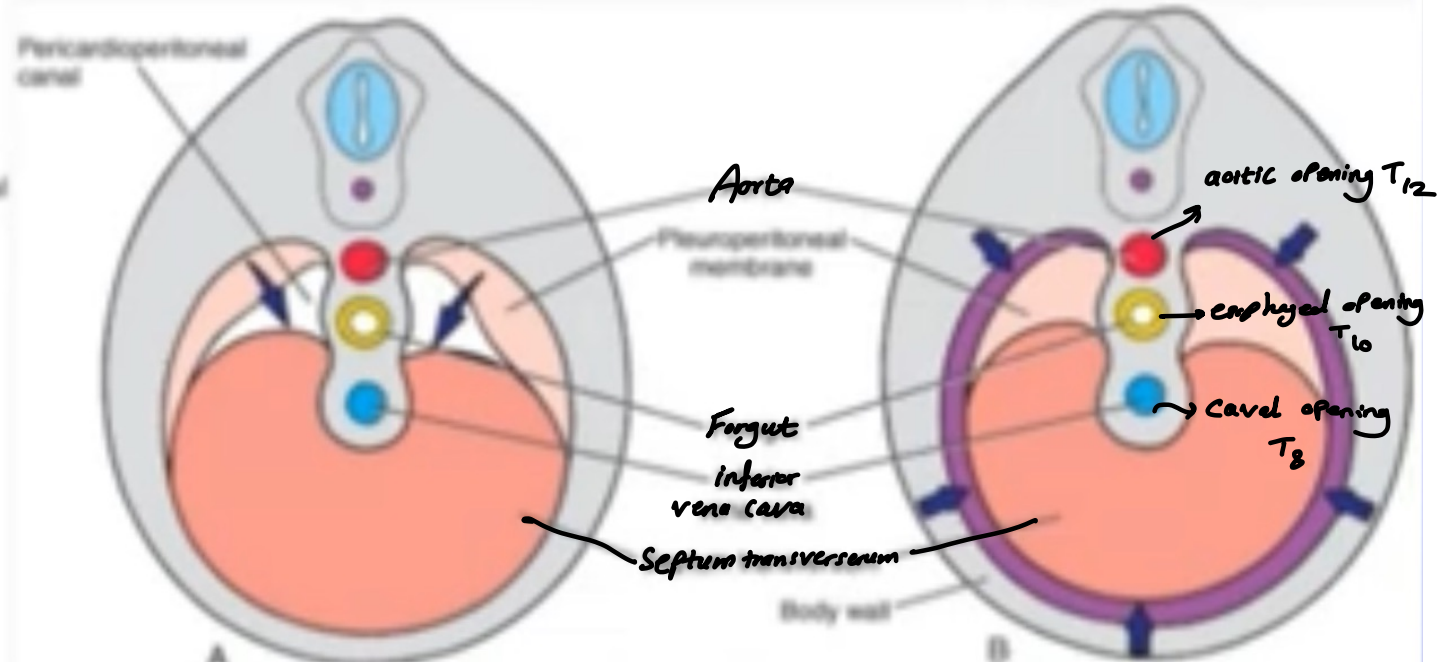
Separating the abdominal and thoracic cavities:

development of the septum transversum and diaphragm

→ thoracic cavity
→ abdominal cavity
→ 3 فتحات تفتح بين
→ بطع



Schneider et al. Human Embryology, 4th Edition.
Copyright © 2008 by Churchill Livingstone, an imprint of Elsevier Inc. All rights reserved.

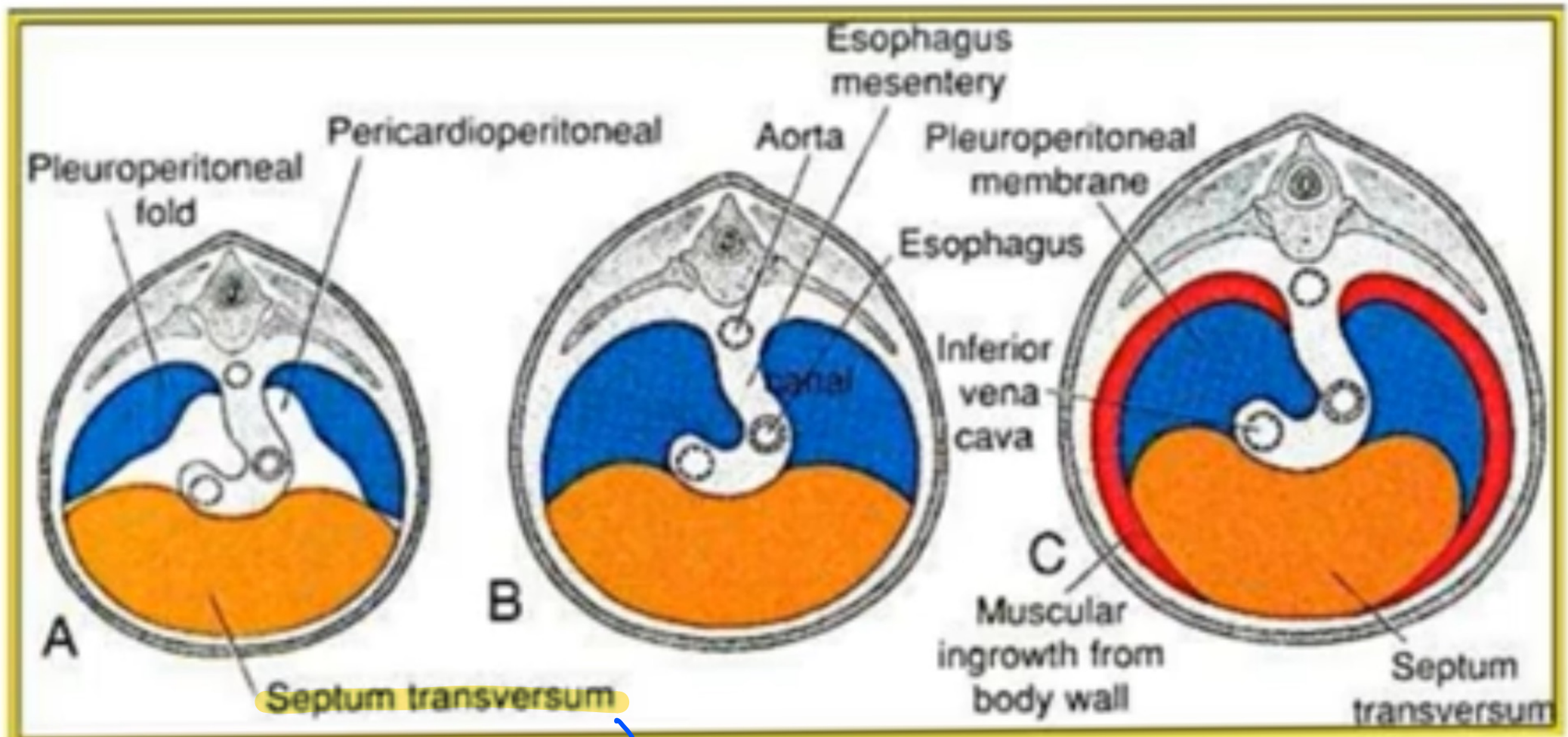


Schneider et al. Human Embryology, 4th Edition.
Copyright © 2008 by Churchill Livingstone, an imprint of Elsevier Inc. All rights reserved.

- The septum transversum stops at the gut tube, leaving two open passageways on the left and right sides, the "pericardioperitoneal canals" (shown on the left)
- Closing off these canals requires growth from the dorsolateral body wall, aka the "pleuroperitoneal membranes" (shown on the right)
- Defects in this process cause CDH (congenital diaphragmatic hernias): abdominal contents herniate into pleural cavities and interfere with lung development.

DEVELOPMENT OF DIAPHRAGM

یہ اسم معروف رانہ بطلعہ *Septum transversum*

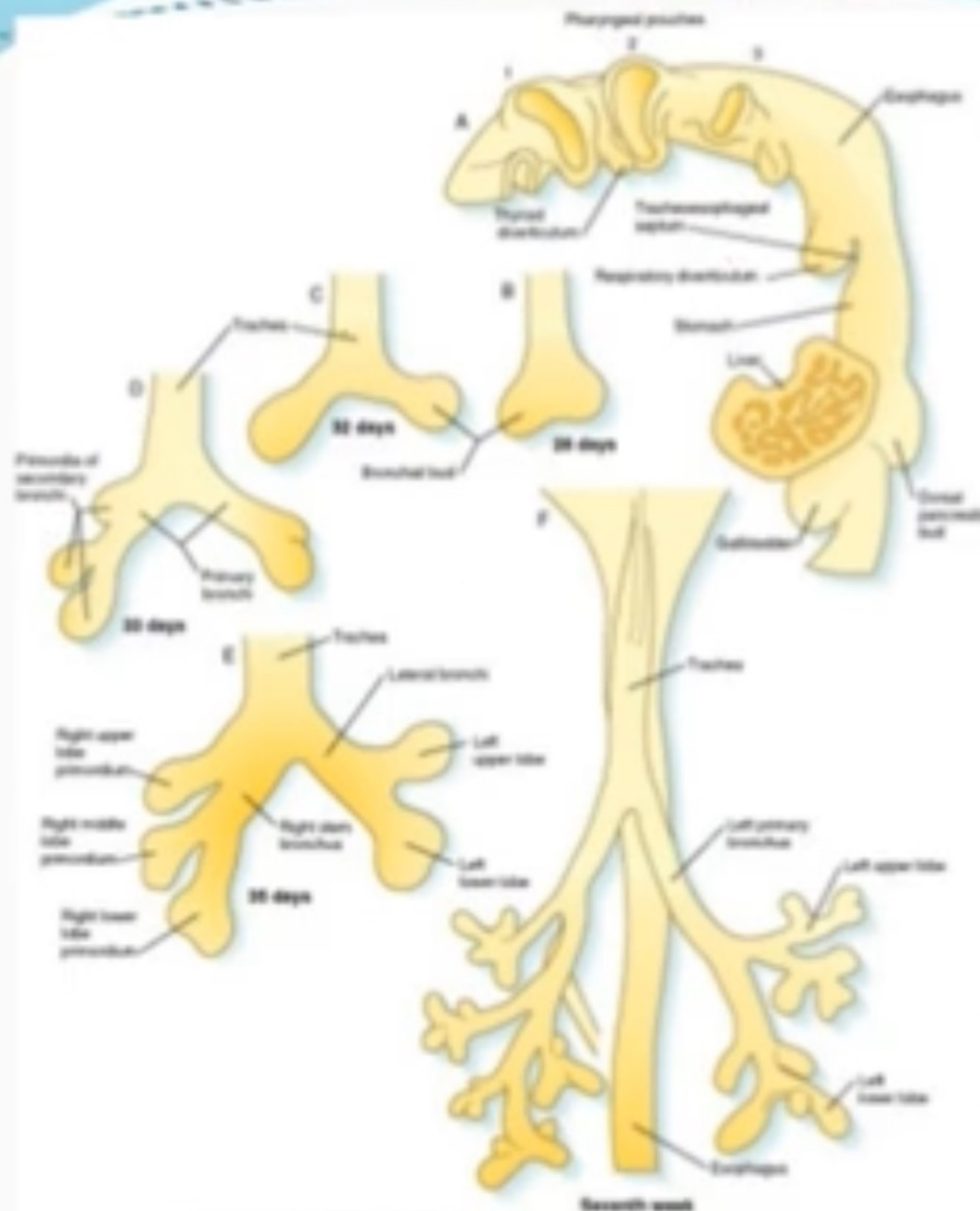


یہ بھل جزیرہ *Septum transversum* ہے
مشت سے ملتی ہے

Initial Patterning of the Lung:

First three branching events are stereotyped:

After the initial bifurcation into two primary bronchi, two buds, or secondary bronchi, form on the left and three on the right predicting the five lobes of the adult human lung. Ten tertiary (segmental) bronchi form in the right lung and eight in the left lung - establishing the bronchopulmonary segments of the adult human lung.

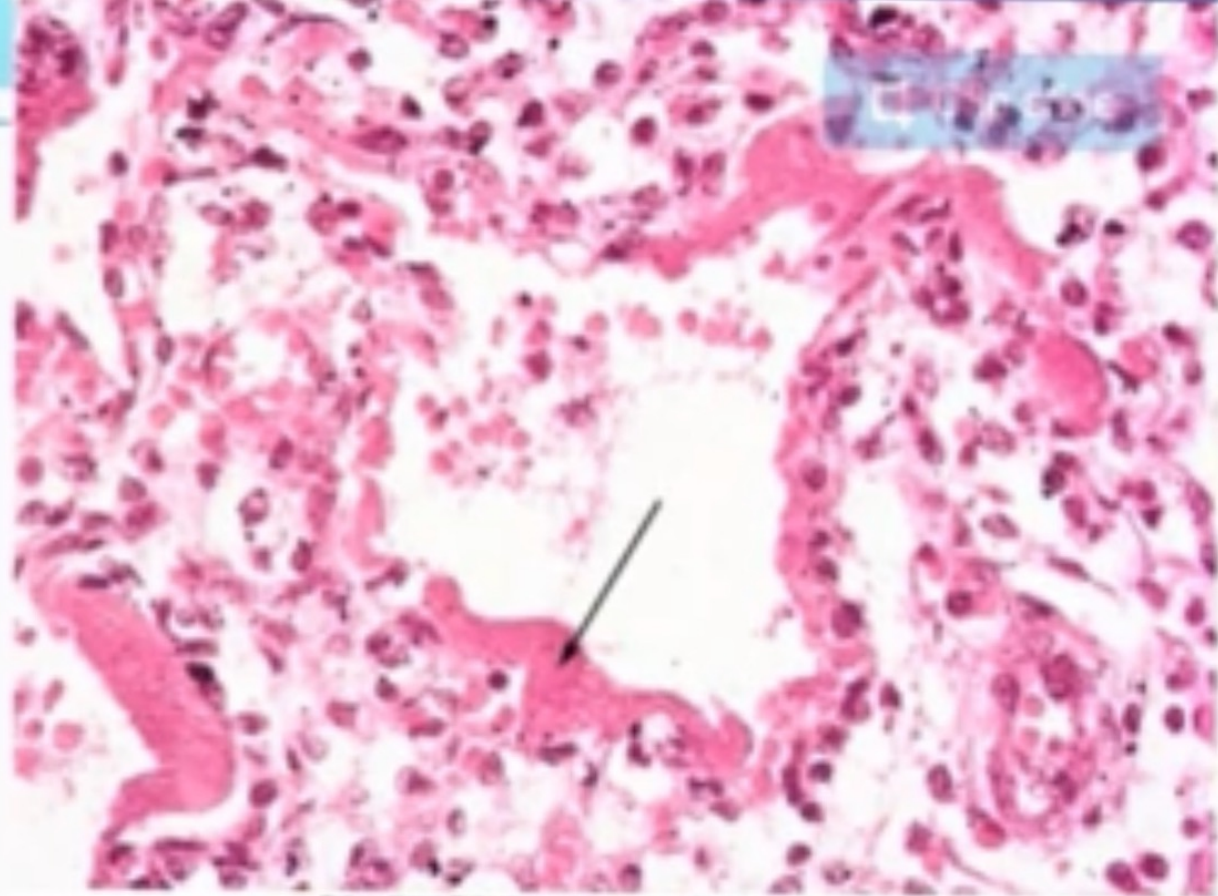


Clinical Correlations:

صعوبة التنفس بسبب انخفاض سطح التوتر السطحي في الحويصلات الهوائية

Respiratory Distress Syndrome (RDS) / Hyaline Membrane Disease: (HMD)

This disease affects 2% of live newborn infants, with prematurely born being most susceptible. 30% of all neonatal disease results from HMD or its complications.



Carlson: Human Embryology and Developmental Biology, 4th Edition.
Copyright © 2009 by Mosby, an imprint of Elsevier Inc. All rights reserved.

① ↑ Type 2 Pneumocytes

* Surfactant deficiency is the major cause of RDS or HMD. The lungs are underinflated and the alveoli contain a fluid of high protein content, probably derived from circulation substances and injured pulmonary epithelium.

②

In addition to prematurity, prolonged intrauterine asphyxia may produce irreversible changes in Type II alveolar cells, rendering them incapable of producing surfactant. Other factors may contribute to surfactant deficiency, but the genetics of surfactant production are not well-defined.

Prolonged, labored breathing damages alveolar epithelium, leading to protein deposition, or "hyaline" changes (shown in figure).

* صدمة الرئة الناتجة عن ICU وممكنه يعطوه artificial surfactant، يتجلبه breathing وممكنه يمدى وممكنه لا.

Clinical Correlations:

Congenital Lung Cysts:

کتیه

Cysts (filled with fluid or air) are thought to be formed by the dilation of terminal bronchi, probably due to irregularities in later development. If severe, cysts are visible on radiographs. Highly variable outcomes result from different cystic conditions.

Agnesis of the Lungs:

absence of lung

ممتنع بیدی
baby

Can occur bilaterally or unilaterally. Unilateral lung agenesis is compatible with live as remaining side hyperexpands and compensates.

Lung Hypoplasia:

Small lung

mild → ممتنع بیدی
extreme → صیدت

غالباً
تولد معاً

Often caused by congenital diaphragmatic hernias or congenital heart disease. Characterized by reduced lung volume. Extreme hypoplasia is inconsistent with life.